AM1 Molecular Orbital Study of the Transmission of Electronic Effects in the 5-Membered Heteroaromatics: Proton and Hydride Ion Affinities of 4- and 5-Substituted (2-Heteroaromatic)methyl Anions and Cations

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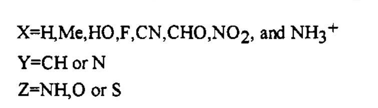
The proton and hydride ion affinities of a series of the benzyl-like anions and cations of 4- and 5-substituted 2-methyl 5-membered heteroaromatic compounds have been calculated by the semiempirical AM1 MO method. Calculations included para- and meta-substituted toluenes, similarly substituted 1,3-pentadienes, and 3-aza-1,3-pentadienes as various models for the possible pathways for the effect of the substituents to be transmitted to the reaction site. There was excellent correlation between the 4-substituted compounds and the *m*-toluenes and between the 5-substituted compounds and the *p*-toluenes. Compared to the other ring atoms, substituents at either the 4- or 5-position have little effect on the change in the charges on the heteroatoms in going to either the cation or anion of the heteroaromatic compounds. It was concluded that transmission of electronic effects is primarily through the carbon skeleton with little if any through the heteroatom.

The effect of substituents on rates of reaction and equilibria is one of the principal concerns of physical organic chemistry, and an understanding of the method(s) by which such effects are transmitted from the substituent to the reaction center has been the object of many studies.[1] Contrary to the situation with 6-membered rings, the odd number of atoms in the 5-membered heteroaromatic compounds allows two different pathways for the transmission of electronic effects through the molecules, one with an odd number of intervening atoms and the other an even number. It is known from the pK_a's of 5-membered heteroaromatic 2-carboxylic acids that substituents at the 4-position behave like meta-substituents on benzene (*i.e.*, follow meta-σ values) while substituents at the 5-position are like para-substituents (*i.e.*, para-σ values).[2] The rates of solvolysis of 5-substituted 1-(2-furyl, 2-thienyl, 2-thiazolyl, or 1-methyl-2-imidazolyl)-ethyl *p*-nitrobenzoates or chlorides follow $\sigma_p{}^+$ values of the substituents but $\sigma_m{}^+$ or σ_m give a less satisfactory correlation.[3] Two models have been proposed to explain how electronic effects are transmitted through the 5-membered heteroaromatics. (1) The "pseudovinyl" model considers the heteroatom to behave as a –CH═CH– unit in benzene and thus allows transmission through the heteroatom. (2) The alternative view considers the heteroatom as being isolated due to the single-bond character of the bonds to C2 and C5; electronic effects are only transmitted through the carbon chain.[4] In this case the effect should depend upon the aromaticity of the heteroaromatic; *i.e.*, only those systems of low aromaticity, such as furan, where there is more bond localization, should follow this model.

Unfortunately, other experimental data regarding substituent effects are either for electrophilic substitution on the ring, where the electronic structure of the intermediate is completely changed, or physiochemical data such as IR stretching frequencies, oxidation potentials, NMR chemical shifts, NH acidity, or photoelectron spectra.[5] From CNDO calculations on 4- and 5-substituted pyrroles, furans, and thiophenes and their conjugate acids, Belen'kii, Abronin, and co-workers have correlated the localization energies for 2-protonation with the σ^+ values for the substituents; ($\sigma_m{}^+$ for the 4-substituents and $\sigma_p{}^+$ for the 5-substitutents).[6] The localization energies for 2-protonation are more sensitive to substitution at the 4-position than at the 5-position. The order of sensitivity to substitution is furan > pyrrole > thiophene. However, as indicated above, the formation of the conjugate acids completely changes the electronic structure with the rehybridization of the C2 carbon atom and cancellation of the aromatic character of the ring system.

Thus, it was of interest to investigate theoretically the transmission of electronic effects through the aromatic ring to a side chain so as to retain the aromaticity of the ring system. The particular approach chosen was to investigate the effect of substituents on proton and hydride ion affinities and electronic charges in the 2-methyl 5-membered heteroaromatics.



(1)

X=H,Me,HO,F,CN,CHO,NO_2, and $NH_3{}^+$
Y=CH or N
Z=NH,O or S

Fiorenza *et al.* carried out *ab initio* calculations at the STO-3G level (without optimization) for the change in σ, π, and total charge at both the ring and side-chain heavy

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[•] Abstract published in *Advance ACS Abstracts,* November 1, 1993.

[1] Johnson, C. D. *The Hammett Equation*; Cambridge Univ. Press: London, 1973.

[2] Jaffe, H. H.; Jones, H. L. *Adv. Heterocycl. Chem.* **1964**, *2*, 209. Exner, O.; Simon, W. *Collect. Czech. Chem. Commun.* **1964**, *29*, 2016. Melent'eva, T. A.: Kazanskaya, L. V. ; Berezovskii, V. M. *Dokl. Akad. Nauk SSSR* **1967**, *175*, 354 (Engl. transl. 624). Fringuelli, F.; Marino, G.; Savelli, G. *Tetrahedron* **1969**, *25*, 5815. Thomasik, P.; Johnson, C. D. *Adv. Heterocycl. Chem.* **1976**, *20*, 1.

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[4] Marino, G. *Adv. Heterocycl. Chem.* **1971**, *13*, 235. Katritzky, A. R.; Taylor, R. *Ibid.* **1990**, *47*, 132.

Table I. AM1 Proton Affinities (kcal/mol) of the Anions from Substituted Toluenes, 1,3-Pentadienes, 3-Azapenta-1,3-dienes, and Cyclopentadienyl Anions[a]

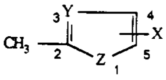
	toluenes		1,3-pentadienes		3-azapenta-1,3-dienes		
substituents	*p*-	*m*-	5-	4-	5-	4-	cyclopentadienyl anions
H	373.6	373.6	370.1	370.1	363.7	363.7	509.2
Me	372.6	373.8	368.9	370.8	362.5	365.0	505.9
OH	373.4	369.5	370.4	364.8	363.9	357.6	503.8
F	367.7	366.8	364.0	362.5	357.1	355.8	502.2
CN	355.5	362.7	348.4	358.6	341.8	352.5	488.5
CHO	355.2	365.9	346.4	362.4	340.3	354.9	484.0
NO_2	342.5	357.8	331.4	350.5	325.3	344.6	473.9
NH_3^+	271.7	280.9	259.8	269.0	253.1	262.7	412.7

[a] ΔH_f (H^+) = 367.21 kcal/mol.

atoms in going from toluene, 2-methylfuran, and 2-methylthiophene to their respective anions.[7]

Experimental Section

Dewar's AM1 semiempirical MO method was used to calculate the heats of formation and charges in the 4- and 5-substituted 2-methylpyrroles, furans, thiophenes, imidazoles, oxazoles, and thiazoles **1** and their benzyl-like anions.[8] In addition, the corresponding cations of the 2-methylpyrroles, furans, and thiophenes were included along with the unsubstituted 2-methylimidazoles, oxazoles, and thiazoles.



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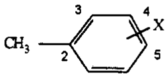

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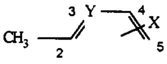

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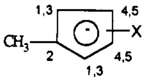

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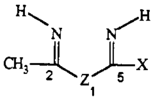

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The AM1 method has been shown to give reasonable values for proton affinities of heterocycles.[9] The substituents were methyl, hydroxyl, fluoro, cyano, formyl, nitro, and the positively charged ammonium groups. The bond angles and distances were optimized while keeping the ring planar. As reference compounds, the meta- and para-substituted toluenes **2**, 1- and 2-substituted penta-1,3-dienes, and 3-azapenta-1,3-dienes **3**, forced to be cisoid planar, and both their anions and cations were included. (So as to prevent confusion in the tables, the carbon atom carrying the methyl group is numbered as the 2-position in each compound; *i.e.*, C_5 in the pentadienes corresponds to the methyl group of the heteroaromatics.) In the anions and cations of all compounds, the CH_2 group was forced to be coplanar with the ring. The hydroxyl and formyl groups gave problems in that in some cases optimization resulted in noncoplanarity; also, when forced to be coplanar there are two possible conformations for these groups. Calculations were made for both conformations, and the results for the lower energy conformer were selected. To remove the effect of the heteroatom, calculations were also done on 3-substituted methylcyclopentadienyl anions **4**, their dianions (loss of an additional proton from the methyl group), and fulvenes (corresponding to the cations from the methylcyclopentadienyl anions). As a model for the heteroatom system, calculations on the similarly substituted MeC(=NH)ZC(=NH)X **5**, where Z = NH, O, or S and the molecules were constrained to be coplanar, were included.

In the case of the pyrroles and imidazoles, it was found that the N–H bonds in the benzyl-like anions were directed at *ca.* 49–55° from coplanarity. (This bending was confirmed by *ab initio* calculations at the STO-3G level.[10]) The bending, which reduced the heats of formation by about 3 kcal/mol, was slightly more pronounced in the imidazoles and for the 5-substituted pyrroles and imidazoles. Likewise, the Z–C2 and Z–C5 bonds were elongated more in going from neutral to anion than in furan or oxazole. Thus, in these anions, the N has an increased sp^3 character which has an important effect on the charge distribution in these compounds as compared to the other systems. This effect is specific for a heteroatom carrying a hydrogen atom since all of the ring hydrogen atoms in the dianions resulting from deprotonation of the methylcyclopentadienyl anion were in the plane of the ring.[11]

Correlation analysis and graphical visualization of the data were done using the QuattroPro program.[12]

Table II. AM1 Proton Affinities (kcal/mol) of the Anions from Substituted 2-Methyl 5-Membered Single Heteroatom Heteroaromatics

	pyrrole		furan		thiophene	
substituents	5-	4-	5-	4-	5-	4-
H	379.7	379.7	372.5	372.5	369.2	369.2
Me	378.1	379.5	371.9	372.6	368.0	369.4
HO	378.7	373.5	369.7	366.9	370.1	364.0
F	372.6	371.9	366.2	364.7	362.3	362.0
CN	350.6	369.0	352.6	360.7	350.0	358.3
CHO	359.9	373.7	350.9	363.6	349.1	361.5
NO_2	344.8	361.9	337.0	352.8	335.4	351.0
NH_3^+	266.6	289.9	258.1	278.2	262.1	277.2

Proton and Hydride Ion Affinities

Proton and hydride ion affinities were calculated from the difference between the heats of formation of the neutral compounds and their ions (Tables I–VII). With the exception of the *m*- and *p*-NH_3^+ compounds, the proton affinities of the benzyl anions correlate surprisingly well with σ^- values (r = 0.908) as do the hydride ion affinities with σ^+ values (r = 0.883) considering that the σ-values were obtained in solution.[13] Thus, it is not unexpected that there is a good correlation between the proton and

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(5) Lopyrev, V. A.; Larina, L. I.; Vakul'skaya, T. I. *Usp. Khim.* **1986**, *55*, 769 (Engl. transl. 411).

(6) Gorb, L. G.; Morozova, I. M.; Belen'kii, L. I.; Abronin, I. A. *Izv. Akad. Nauk SSSR* **1983**, *828* (Engl. transl. 755).

(7) Fiorenza, M.; Ricci, A.; Sbrana, G.; Pirazzini, G.; Eaborn, C.; Stamper, J. G. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1232.

(8) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. Stewart, J. J. P. *QCPE* no. 455, revision 6.

(9) Dewar, M. J. S.; Dieter, K. M. *J. Am. Chem. Soc.* **1986**, *108*, 8075. Meot-Ner, M.; Liebman, J. F.; Kafafi, S. A. *Ibid.* **1988**, *110*, 5937. Meot-Ner, M.; Kafafi, S. A. *Ibid.* **1988**, *110*, 6297. Carmona, C.; Hidalgo, J.; Marcos, E. S.; Pappalardo, R. R.; Munoz, M.; Balon, M. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1881.

(10) Gaussian 90, Revision I: Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. Gaussian, Inc., Pittsburgh PA, 1990.

(11) AM1 results for the anion of 2-methylphosphole and the "onium" tautomers of 2-methylfuran and thiophene, in which a proton is transferred from the methyl group to the oxygen or sulfur atom, also shows bending of the hydrogen attached to the heteroatom.

(12) QuattroPro, Borland International, 1800 Green Hills Road, P.O. Box 66001, Scotts Valley, CA 95066.

(13) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

Table III. AM1 Proton Affinities (kcal/mol) of the Anions from Substituted 2-Methyl 5-Membered Two Heteroatom Heteroaromatics

	imidazole		oxazole		thiazole	
substituents	5-	4-	5-	4-	5-	4-
H	374.7	374.7	366.9	366.9	361.7	361.7
Me	372.9	374.4	366.6	367.4	360.8	362.6
HO	372.7	368.3	365.6	361.7	358.6	357.2
F	366.8	365.9	360.3	358.8	354.7	354.4
CN	353.7	363.5	347.1	355.3	342.8	351.5
CHO	355.0	367.6	345.9	355.3	343.2	355.5
NO_2	339.0	355.5	331.5	347.4	328.1	344.3
NH_3^+	260.6	284.3	257.8	273.5	253.8	269.9

Table IV. AM1 Proton Affinities (kcal/mol) of the Anions from Substituted MeC(=NH)ZC(=NH)X

substituents	Z = NH	Z = O	Z = S
H	376.4	372.5	365.5
Me	377.4	373.7	366.8
OH	373.3	365.9	348.1
F	370.3	365.1	353.6
CN	368.6	364.0	346.6
CHO	373.5	370.1	350.8
NO_2	362.2	357.0	335.1
NH_3^+	292.8	*a*	264.7

[a] Species not stable.

Table V. AM1 Hydride Ion Affinities (kcal/mol) of the Cations from Substituted Toluenes, 1,3-Pentadienes, and Fulvenes[a]

	toluenes		1,3-pentadienes		
substituents	*p*-	*m*-	5-	4-	fulvenes
H	241.0	241.0	236.4	236.4	80.0
Me	236.3	239.8	230.4	235.7	80.6
OH	232.9	244.2	224.7	241.7	82.4
F	241.4	248.1	235.7	245.9	87.5
CN	250.0	249.5	245.9	245.7	99.4
CHO	248.7	245.8	244.9	240.7	98.2
NO_2	260.1	256.1	254.6	252.2	113.1
NH_3^+	331.5	330.6	330.3	334.2	188.8

[a] ΔH_f (H^-) = 33.23 kcal/mol.

Table VI. AM1 Hydride Ion Affinities (kcal/mol) of the Cations from Substituted 2-Methyl 5-Membered Single Heteroatom Heteroaromatics

	pyrrole		furan		thiophene	
substituents	5-	4-	5-	4-	5-	4-
H	224.1	224.1	204.3	204.3	199.6	199.6
Me	219.3	222.2	198.1	203.4	195.8	198.1
HO	217.9	225.5	193.8	206.6	193.4	201.6
F	228.0	231.6	205.8	212.3	203.5	206.5
CN	236.7	234.9	215.1	214.3	209.9	208.7
CHO	234.5	231.6	213.3	210.9	207.7	205.4
NO_2	248.5	243.8	226.2	222.5	220.4	216.1
NH_3^+	329.8	323.1	307.3	302.2	298.2	290.9

Table VII. AM1 Hydride Ion Affinities (kcal/mol) of the Cations from Substituted MeC(=NH)ZC(=NH)X

substituents	Z = NH	Z = O	Z = S
H	282.9	285.8	282.2
Me	281.5	283.8	279.6
OH	285.3	289.0	284.9
F	288.8	292.0	288.4
CN	289.0	292.0	288.0
CHO	283.9	285.7	285.2
NO_2	292.9	295.6	291.3
NH_3^+	361.8	368.2	362.9

Table VIII. Correlation of AM1 Proton Affinities of the Anions from Substituted 2-Methyl Heteroaromatics and Open-Chain Compounds with the Anions from Substituted Toluenes

	r	slope[a]
pyrrole		
4-substituted	0.999 meta	0.964 (0.011)
5-substituted	0.993 para	1.102 (0.038)
furan		
4-substituted	0.999 meta	1.009 (0.043)
5-substituted	0.999 para	1.118 (0.007)
thiophene		
4-substituted	0.999 meta	0.990 (0.016)
5-substituted	0.999 para	1.053 (0.005)
imidazole		
4-substituted	0.999 meta	0.941 (0.013)
5-substituted	0.999 para	1.111 (0.046)
oxazole		
4-substituted	0.999 meta	1.015 (0.008)
5-substituted	0.999 para	1.071 (0.010)
thiazole		
4-substituted	0.999 meta	0.995 (0.011)
5-substituted	0.999 para	1.051 (0.008)
cyclopentadienyl anion	0.993 para	0.926 (0.033)
1,3-pentadiene		
4-substituted	0.999 meta	1.092 (0.012)
5-substituted	0.997 para	1.087 (0.035)
3-azapenta-1,3-diene		
4-substituted	0.999 meta	1.087 (0.012)
5-substituted	0.997 para	1.088 (0.029)
MeC(=NH)ZC(=NH)X		
Z = NH	0.998 meta	0.913 (0.020)
Z = O[b]	0.844 meta	0.821 (0.110)
Z = S	0.973 meta	1.038 (0.058)

[a] Errors in parentheses. [b] Only seven points used.

hydride ion affinities for the benzyl ions; r = 0.983 (including the *m*- and *p*-NH_3^+ groups). Karaman *et al.* calculated the hydride ion affinities of 16 meta- and para-substituted benzyl cations using the MNDO MO method.[14] They found that there was a good correlation of the hydride ion affinities with the corresponding σ^+ values (r = 0.977). However, their compounds did not include the CHO, NO_2, or NH_3^+ substituents. For all of the systems considered here, with the exception of some of the open chain CZC systems, both the proton and hydride ion affinities correlate very well with those of the similarly substituted toluenes (Tables VIII and IX). As found experimentally for the pK_a's of the 2-carboxylic acids, the proton affinities of the 5-substituted compounds correlate with the para-substituted toluenes and the 4-substituted compounds with the meta-substituted toluenes. In most cases the correlation coefficient was >0.999. The slope of the correlation line was *ca.* 1. The order of increasing proton affinities for the 5-(or para-)substituted compounds is H ~ OH < Me < F< CN ~ CHO < NO_2 < NH_3^+, while for the 4-(or meta-)substituted compounds it is Me < H < OH < F < CHO < CN < NO_2 < NH_3^+. This was also the case for the pentadienes and the 3-azapentadienes. Similarly, hydride ion affinities for the heteroaromatic cations correlate well with the benzyl cations; the 5-substituted cations follow the para-substituted benzyl cations and the 4-substituted cations with the *m*-benzyl cations. This is in agreement with the results for the solvolysis of the 1-(2-heteroaromatic)ethyl compounds.

The proton affinities of methylcyclopentadienyl dianions correlate with *p*-toluenes (r = 0.994) rather than with the *m*-toluenes (r = 0.948). Thus, they tend to resemble the 5-substituted heteroaromatics rather than the 4-substituted. This is also the case for the hydride ion affinities of the fulvenes. For the MeC(NH)ZC(NH)X systems,

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[14] Karaman, R.; Huang, J.-T. L.; Fry, J. L. *J. Org. Chem.* **1991**, *56*, 188.

Table IX. Correlation of AM1 Hydride Ion Affinities of the Cations from Substituted 2-Methyl Heteroaromatics and Open-Chain Compounds with the Cations from Substituted Toluenes

	r	slope[a]
pyrrole		
4-substituted	0.998 meta	1.105 (0.022)
5-substituted	0.992 para	1.148 (0.015)
furan		
4-substituted	0.999 meta	1.090 (0.012)
5-substituted	0.999 para	1.141 (0.009)
thiophene		
4-substituted	0.999 meta	1.020 (0.010)
5-substituted	0.999 para	1.070 (0.016)
fulvene		
	0.989 para	1.126 (0.048)
1,3-pentadiene		
4-substituted	0.999 meta	1.086 (0.013)
5-substituted	0.999 para	1.051 (0.015)
MeC(=NH)ZC(=NH)X		
Z = NH	0.997 meta	0.890 (0.018)
Z = O	0.996 meta	0.932 (0.025)
Z = S	0.997 meta	0.910 (0.020)

[a] Errors in parentheses.

where there are three intervening atoms, the proton affinities correlate with meta-substituted benzyl anions ($r = 0.998$ for Z = NH, 0.844 for Z = O, and 0.982 for Z = S). However, the slopes are more varied; 0.91 for Z = NH, 0.82 for Z = O, and 1.04 for Z = S. The hydride ion affinities also correlate with those of the meta-substituted benzyl cations rather than para-substituted; $r = 0.997$ for Z = NH, 0.996 for Z = O, and 0.997 for Z = S.

Transmission of substituent effects through the heteroaromatic systems to the side-chain reaction center is essentially independent of the nature of the heteroatom(s). For example, replacement of the hydrogen atom at the 5-position by a nitro group on any of the six 2-methyl heteroaromatics decreases their proton affinities by 35.6 ± 0.9 kcal/mol; for replacement at the 4-position instead, the proton affinities decrease by 18.6 ± 0.8 kcal/mol. Likewise, a nitro group at the 5-position increases the hydride ion affinities by 22.1 ± 1.3 kcal/mol and at the 4-position by 17.6 ± 1.1 kcal/mol. The corresponding decreases in the proton affinities for *p*- and *m*-nitrobenzyl ions are 31.1 and 15.8 kcal/mol; for the hydride ion affinities, the increases are 19.1 and 15.1 kcal/mol, respectively.

Table X. Charge Differences between Neutral and Anions in 2-Methyl Compounds[a]

	Z1	C5	C4	Y3	C2	Me
total charges						
toluene		−228	64	−165	173	−525
pentadiene		−284	151	−342	183	−506
azapentadiene		−293	122	−244	79	−482
cyclopentadiene	−183	−33	−33	−183	354	−766
pyrrole	−15	−250	111	−273	208	−548
furan	−81	−217	87	−283	211	−562
thiophene	−369	−142	103	−287	316	−495
imidazole	−4	−263	91	−225	139	−511
oxazole	−85	−220	64	−227	145	−541
thiazole	−391	−138	89	−237	248	−477
π charges						
toluene		−288	16	−204	94	−416
pentadiene		−369	89	−422	95	−376
azapentadiene		−379	95	−336	2	−356
cyclopentadiene	−215	−63	−63	−215	298	−755
pyrrole	143	−245	90	−312	208	−447
furan	−90	−263	49	−346	141	−474
thiophene	−204	−273	59	−351	169	−389
imidazole	173	−255	95	−254	145	−417
oxazole	−105	−260	53	−276	72	−463
thiazole	−220	−268	65	−285	95	−371
σ charges						
toluene		60	48	39	79	−109
pentadiene		76	62	80	88	−130
azapentadiene		86	27	90	77	−126
cyclopentadiene	32	30	30	31	56	−11
pyrrole	−158	−5	21	39	0	−101
furan	9	56	38	63	70	−88
thiophene	−165	131	44	64	147	−106
imidazole	−177	−8	−4	29	−6	−94
oxazole	20	40	11	49	73	−78
thiazole	−171	130	24	48	53	−106

[a] In millielectrons.

Changes in Charge on Going to Ions

The AM1 program uses Mulliken's population analysis to give both the total electron population on each atom and the s, p_x, p_y, and p_z atomic orbital electron populations.[15] The changes in total, σ, and π charges were calculated as the difference between the populations of the neutral molecule and the ion. A negative value for the change indicates that the charge becomes more negative in the ion. In going from the neutral molecule to the anion, the sign of the change in both the total charge and the π electron population alternates, being negative on the methyl C atom, then positive on C2, again negative on Y3, positive on C4, and negative on C5 (Table X). With few exceptions, the changes in σ charges for the ring atoms are positive. Whereas the change in π charges on the heteroatom is negative when it is either oxygen or sulfur, it is positive for nitrogen. In going from sp^2 to sp^3, electrons are drawn from the π orbitals into the σ orbitals. In the case of sulfur, where there is a high positive charge on sulfur in the neutral thiophene molecule, the large negative change is due to the transfer of σ electrons to C2 and C5 in going to the anion.

Pagani has devised a π electron charge demand parameter using the difference in ^{13}C and ^{15}N chemical shifts in going from the neutral molecules to their anions and has applied this to 2-benzyl-1-methylimidazole and 2-benzyloxazole.[16] The relative order of the change in π electron densities calculated in this manner is in good agreement with those from the AM1 calculations for the 2-methylimidazole and -oxazole and their anions.

As expected, the changes in going from the neutral to the cations are in most cases opposite to those found for the anions. The notable exception is that in both cases the σ charges on the benzyl-like carbon atom are negative.

Effect of Substituents on Change in Charge

For the purpose of comparing the effect of substituents, the difference between the change in charge in going from neutral to ion was calculated for the total, π, and σ populations; *i.e.*, $(q_B^{\pm} - q_{HB}) - (q_A^{\pm} - q_{HA})$, where HA is the unsubstituted compound and HB is the substituted compound. As before, a negative value indicated that the

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[15] The sum of the s, p_x and p_y electron populations corresponds to the σ electron population and is equal to the total atomic electron population minus the π electron population. As the molecules are oriented, the π electrons are in the p_z orbital.

[16] Bradamante, S.; Pagani, G. A. *Pure Appl. Chem.* **1989**, *61*, 709. Abbotto, A.; Bradamante, S.; Canavesi, A.; Pagani, G. A. Third International Symposium on Carbanion Chemistry, Gallipoli, Italy, June 1992.

Table XI. Charge Differences between Neutral and Cations in 2-Methyl Compounds[a]

	Z1	C5	C4	Y3	C2	Me
total charges						
toluene		227	−57	170	−125	306
pentadiene		284	−140	366	−133	258
azapentadiene		326	102	277	−176	352
cyclopentadiene	91	125	125	91	157	−46
pyrrole	39	275	−9	203	−26	163
furan	53	298	−42	268	−88	224
thiophene	353	97	−18	158	−116	259
imidazole	92	254	65	169	−69	196
oxazole	93	306	32	209	−115	252
thiazole	494	33	46	127	−184	280
π charges						
toluene		295	−18	213	−112	443
pentadiene		379	−89	463	−115	381
azapentadiene		440	−64	339	−184	494
cyclopentadiene	158	194	194	158	208	74
pyrrole	102	377	29	254	−31	277
furan	64	396	0	328	−115	343
thiophene	228	266	5	194	−73	392
imidazole	168	382	103	161	−110	310
oxazole	133	438	72	200	−193	369
thiazole	346	255	69	103	−162	406
σ charges						
toluene		−67	−39	−42	−13	−137
pentadiene		−94	−51	−97	−18	−122
azapentadiene		−113	−38	−62	7	−139
cyclopentadiene	−67	−69	−69	−67	−52	−120
pyrrole	−63	−102	−38	−51	5	−114
furan	−11	−98	−42	−60	27	−119
thiophene	−126	−170	−22	−36	−43	−133
imidazole	−76	−127	−37	8	41	−144
oxazole	−40	−132	−40	9	78	−117
thiazole	−151	−222	−23	25	−22	−126

[a] In millielectrons.

substituent made the change in charge (from neutral to ion) more negative.

As expected for anions, the change in the total, σ, and π charges on the methyl group becomes more positive with increasing electron withdrawal and correlates well with the change in the charges for the corresponding toluenes ($r > 0.94$). The 5-substituted compounds are slightly more sensitive to substituent effects than are the 4-substituted, while as families, furan and oxazole are most sensitive and pyrrole and imidazole the least sensitive. Likewise for cations, the changes in the charges become more positive with increasing electron withdrawal and correlate with the toluenes.

The effect of substituents on the total, σ, and π charges on the heteroatom is not uniform. There is only consistency between pairs: pyrrole–imidazole, furan–oxazole, and thiophene–thiazole. For both 4- and 5-substitution, the mono heteroatom compounds are more sensitive to the effect of substituents than the corresponding 3-aza species. The effect of substituents on the charge on the heteroatom varies according to the heteroatom. However, the magnitude of the change is much less than that on the other ring atoms.

Conclusions

The near constancy of the slopes for the correlation of the proton and hydride ion affinity data for the 1,3-pentadienes, 3-aza-1,3-pentadienes, and the 2-methyl heterocycles with the similarly substituted toluenes indicates that substituents produce essentially the same effect on the affinities regardless of aromaticity or structure, *i.e.*, lack of the vinyl group or heteroatom. The data for the CZC system shows that the effect of substituents on the position analogous to the 5-position of the 2-methyl heterocycles is transmitted about as effectively as in the other systems, and thus the effects ought to be transmitted through the heteroatom of the ring compounds. However, any transmission through the heteroatom should follow the meta-substituent effects while transmission through the carbon skeleton follows the para-substituent effects. Since the proton and hydride ion affinities of the 5-substituted heteroaromatics, regardless of their aromaticity, correlate so well with the *p*-benzyl affinities, it follows that electronic effects are not appreciably transmitted through the heteroatom else the correlation would be poorer.

Substituents on the heteroaromatic compounds produce essentially the same effect on the proton and hydride ion affinities regardless of the particular heteroatom. The nature of the heteroatom only shifts the values, *i.e.*, the intercept of the correlation line. The presence of the heteroatom produces considerable perturbation of the charges on C2 and C5, as compared to the charges in the open chain dienes, and this may effect the reaction center attached to C2. This, however, does not change the relative effect produced by substituents on the ring. As in the case of pyridine, substitution of the =CH– by =N– has little influence on the effect of substituents on either proton or hydride ion affinities of the 3-aza heteroaromatics or on the charges in these molecules.

Even when there is a major change in the hybridization, as in the anions of pyrrole and imidazole, the change in the charge on the heteroatom itself is relatively insensitive to the substituent as compared to the other ring atoms. This also suggests that there is little, if any, transmission through the heteroatom. Likewise, the elongation of the Z–C2 and Z–C5 bonds in going to the ions is relatively insensitive, as compared to the changes in carbon to carbon bond lengths, to the nature of the substituents.

In conclusion, the AM1 calculations substantiate the view that there is little if any transmission of electronic effects through the heteroatom and that a bridged "butadiene-like" structure best represents the system in spite of known aromatic character of these compounds.[17]

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(17) Katritzky, A. R.; Feygelman, V.; Musumarra, G.; Barczynski, P.; Szafran, M. *J. Prakt. Chem.* **1990**, *332*, 853.