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THE ORIGIN AND NATURE OF THE π-ELECTRON STERIC EFFECT

JOHN P. IDOUX* and DAVID E. SASSER
Department of Chemistry, Florida Technological University, Orlando, FL 32816, U.S.A.

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Abstract—The existence of conformational or steric proximity substituent effects involving π-electrons has been demonstrated in a number of recent reports but the question of whether this effect is due simply to the size of the substituent or to lone pair electrons on the substituent has not been investigated. Relative to this question, pK_a's for an extensive series of 2'- and 4'-substituted-4-aminobiphenyls and for a series of 4'-substituted-2-aminobiphenyls have been determined. The results of this study demonstrate that a π-electron steric effect is operative in the 2'-substituted-4-aminobiphenyls and that it occurs primarily (when possible) via lone pair electron-π electron interactions and not simply via a steric size effect. The pK_a data for the 4'-substituted-2-aminobiphenyls reinforce this conclusion and further demonstrate that 2,4'-resonance is possible in appropriately substituted 2,4'-disubstituted biphenyls. In addition, the relativity of the concept of substituent size and of electron withdrawing or donating character of various groups is illustrated.

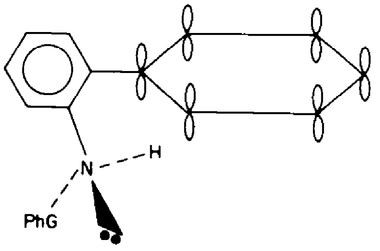
Studies relating to substituent proximity effects have provided a considerable amount of information about the influence of such factors on molecular properties, and many of these studies have produced useful quantitative substituent-property relationships.[1,2] On the other hand, a number of studies have recently been reported which demonstrate the influence of substituent proximity effects which are not explained by quantitative substituent-property correlations. For example, Lambert[3] has shown that the conformational preference of substituted methylenecyclohexanes depends in part on interactions between substituent groups and π-electrons of the *exo*-methylene group, and we have recently demonstrated[4] the influence of π-electron steric interactions on a chemical property.[5] The latter report involved comparative pK_a studies for several substituted aminobiphenyls and indicated that the pK_a's for 4'-substituted-3- and -4-aminobiphenyls could be rationalized in terms of expected, typical substituent effects. However, the pK_a data for the 2'-substituted-4-aminobiphenyl system did not give a quantitative fit via the Hammett equation nor were the order and magnitude of these pK_a's "normal". That is, the 2'-acetamido group had a base weakening effect relative to a base strengthening effect by the 4'-acetamido group, the 2'-hydroxy group was more strongly base strengthening than a 4'-hydroxy or methoxy group and the 2'-nitro group was considerably less base weakening than was a 4'-nitro. These results were attributed to an interaction between a 2'-group and the π-electrons of the adjacent ring carrying the amino group and this interaction was simply called the π-electron steric effect.

Since the report of these results, a question has arisen concerning the origin of the π-electron steric effect as to whether it is due simply to the size of the 2'-group or to lone pair electrons on the 2'-group. In an effort to clarify this question, we have investigated an additional extensive series of 2'- and 4'-substituted-4-aminobiphenyls and, for comparison, a series of 4'-substituted-2-aminobiphenyls.

RESULTS AND DISCUSSION

The pK_a's for the 2'- and 4'-substituted-4-aminobiphenyls are reported in Table 1 and those for the 4'-substituted-2-aminobiphenyls are given in Table 2.

Inspection of the data in Table 1 indicates that the pK_a's for the 4'-substituted-4-aminobiphenyls are "normal" in their direction and magnitude while those for the 2'-substituted series demonstrate the operation of a π-electron steric effect which occurs primarily (when possible) via lone pair electron-π electron interactions and not simply via a steric size effect. For example, the pK_a's for the 2'- and 4'-phenyl derivatives are essentially identical in spite of the potential for significant steric interactions in the case of the 2'-phenyl compound. For the benzamide and sulfonamide derivatives, the amide group is sterically prohibited from exerting its normal resonance electron donating effect in the 2'-position but can assume a minimal-repulsive, non-resonance conformation with respect to the π-electrons of the adjacent ring carrying the amino group (Structure I). As a result, a 2'-amide group can effectively exert only its electron withdrawing inductive/field effect which renders the 2'-amide compounds weaker bases than the parent. These, and the previously reported[4] 2'-acetamido derivatives, are the only examples of an aromatic amine system, of which we are aware, in which an amide group causes a decrease in basicity relative to the parent compound. On the other hand, the 4'-amide compounds demonstrate "normal" substituent effects such that their pK_a's, as expected, are greater than that of the parent compound.



G = CO or SO_2

I

In the case of the carbmethoxy compounds, both, as expected, are weaker bases than the parent. However, the 2'-carbmethoxy group causes a significantly smaller base weakening effect than expected. Relative to the 4'-carbmethoxy derivative, this result is initially rather

Table 1. pK_a's for 2'- and 4'-substituted-4-aminobiphenyls in 50% ethanol–water at 20°

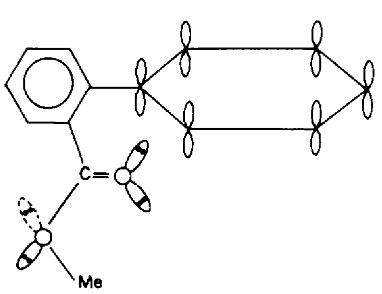
Substituent	pK_a	Substituent	pK_a
H	4.05[a]	2'-COOMe	3.91
H	3.94[b]	4'-COOMe	3.59
2'-Ph	4.01[c]	2'-OCOMe	4.00
4'-Ph	4.02[c]	2'-Cl	4.08
2'-NHCOPh	3.88[c]	4'-Cl	4.00
4'-NHCOPh	4.03[c]	2'-Br	4.12
2'-NHSO$_2$Ph	3.98	4'-Br	4.00
4'-NHSO$_2$Ph	4.34		

[a]In 50% ethanol: D. J. Byron, G. W. Gray and R. C. Wilson, J. Chem. Soc. (C) 831 (1966). [b]In 70% ethanol: P. H. Grantham, E. K. Weisburger and J. H. Weisburger, J. Org. Chem. 26, 1008 (1961). [c]In 70% ethanol.

Tabel 2. pK_a's for 4'-substituted-2-aminobiphenyls in 10% ethanol–water at 20°

Substituent	pK_a	Substituent	pK_a
H	3.78	OMe	3.89
NHAc	3.96	COMe	3.44
Br	3.73	COOMe	3.46
OH	3.84	NO$_2$	3.20

surprising when one considers the small transmission coefficient (0.23–0.24) for the 1,1' bond in a 4'-substituted-4-aminobiphenyl.[7] However, these differences can be accounted for on the basis of a π-electron steric effect. That is, the 2'-carbmethoxy group is sterically prohibited from exerting its normal resonance electron withdrawing effect and at the same time, unlike the various amide derivatives, cannot assume a repulsion-free, non-resonance conformation with respect to the π-electrons of the adjacent ring. (Structures II and III). As a consequence, unshared electron pairs in the 2'-carbmethoxy group interact with the π-electrons of the adjacent ring and cause a displacement of the π-electrons toward the amino group. This interaction has the result of offsetting the electron withdrawing inductive/field effect of the 2'-carbmethoxy group and thus renders the compound significantly more basic than expected.



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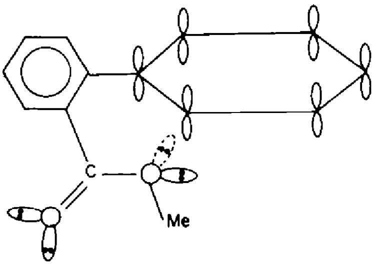

III

The 2'-acetate derivative shows a π-electron effect similar to the 2'-carbmethoxy compound and again has a pK_a which is surprisingly high relative to that of the parent compound if considered only in terms of the "normal" substituent effect of an acetate group. The halogen substituted derivatives also show similar but smaller effects. That is, the 2'-bromo and -chloro derivatives are slightly more basic and the 4'-halo derivatives slightly less basic than the parent compound. The 4'-halo derivatives show the "normal", expected base weakening effect while the 2'-halo isomers are the only examples of an aromatic amine system of which we are aware where a halogen substituent causes an increase in basicity relative to the parent compound.

The data reported in Table 2 for the 4'-substituted-2-aminobiphenyls were determined in order to assess what influence, if any, the reaction site itself has on a π-electron steric effect and also to demonstrate that a 2,4'-disubstituted biphenyl can experience 2,4'-resonance interaction. Inspection of this data indicates that the order and magnitude of the pK_a's for this series, like those for the 4'-substituted-4- and -3-aminobiphenyl series, are "normal" when rationalized in terms of typical substituent effects. That is, the acetamido, methoxy and hydroxy substituents cause expected increases in basicity while the bromo, carbmethoxy, acetyl and nitro substituents cause expected decreases in basi-

Table 3. ΔpK_a's for 2′-substituted-4-aminobiphenyls and 4′-substituted-2-aminobiphenyls

Substituent	ΔpK_a[a] 2′-Substituted Series	ΔpK_a[a] 4′-Substituted Series
NHAc	+0.08[b]	-0.18
OH	-0.12[b]	-0.06
Br	-0.07	+0.05
COOMe	+0.14	+0.32
NO_2	+0.27[b]	+0.58
COMe	--	+0.34
OCOMe	+0.05	--

[a] ΔpK_a = pK_a of parent compound - pK_a of substituted compound.

[b] pK_a's from ref. 4.

city. Further, the ΔpK_a ($\Delta pK_a = pK_a$ of parent compound $-pK_a$ of substituted compound) shown in Table 3 clearly demonstrate the diminished or reversed substituent effects for the 2′-substituted-4-aminobiphenyls relative to the 4′-substituted-2-aminobiphenyls. In addition, as shown by eqn (1), the pK_a data for the 4′-substituted-2-aminobiphenyls provide a reasonably good quantitative

$$pK_a = 3.83 - 0.49\sigma_I - 0.59\sigma_R\ , \quad R = 0.973,\ s = 0.086 \qquad (1)$$

relationship via the dual substituent parameter Hammett equation.[9] As indicated by the coefficients of σ_I and σ_{R^-} in eqn (1), resonance effects play an important role in this series relative to simple polar effects. In fact, as shown by the ρ_{R^-}/ρ_I ratio of 1.20, the 4′-substituted-2-aminobiphenyls are particularly sensitive to resonance effects relative to the 4′-substituted-4-aminobiphenyls ($\rho_{R^-}/\rho_I = 0.89$) and the 4′-substituted-3-aminobiphenyls ($\rho_{R^-}/\rho_I = 0.58$).[10]

The overall results of this and the previously reported study[4] demonstrates the operation of a π-electron steric effect in the 2-substituted biphenyl system and illustrate as well the relativity of the concept of substituent size and of electron withdrawing or donating character of various groups. In addition, it is expected that such effects may well be observed in similar systems such as Lambert[3] has previously demonstrated for certain cyclohexyl derivatives and Bowden[6] for appropriately substituted 1-naphthoic acids.

EXPERIMENTAL

The fourteen 2′- and 4′-substituted-4-aminobiphenyls and seven of the 4′-substituted-2-aminobiphenyls were prepared as previously reported in the literature or by usual, modified procedures and were recrystallized or vacuum distilled to constant melting or boiling points in agreement with the values reported previously.[11] The eighth 4′-substituted-2-aminobiphenyl (i.e. the 4′-acetyl derivative) was prepared by Sn/HCl reduction of 4′-acetyl-2-nitro-biphenyl and had m.p. 82–83.5° (from ethyl alcohol-water). (Calc. for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.41; H, 6.23, N, 6.41%).

The pK_a's reported in Tables 1 and 2 represent the average of at least four determinations and were determined as described previously.[12] The maximum deviation from the mean of replicate pK_a values did not exceed 1.4% except for 2′-chloro-4-aminobiphenyl (1.7%) and 2′-benzamido-4-aminobiphenyl (2.6%).

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REFERENCES

[1] R. W. Taft, In *Steric Effects in Organic Chemistry* (Edited by M. S. Newman), Chap. 13. Wiley, New York (1956).

[2a] O. Exner. In *Advances in Linear Free Energy Relationships* (Edited by N. B. Chapman and J. Shorter), Chap. 1. Plenum Press, New York (1972); [b] J. Shorter, *Ibid.* Chap. 2; [c] M. T. Tribble and J. G. Traynham, *Ibid.* Chap. 4.

[3] J. B. Lambert, R. R. Clikeman and E. S. Magyar, *J. Am. Chem. Soc.* **96**, 2265 (1974).

[4] J. P. Idoux, V. S. Cantwell, J. Hinton, S. O. Nelson, P. Hollier and R. Zarrillo, *J. Org. Chem.* **39**, 3946 (1974).

[5] Similar, though not necessarily π-electron steric, effects have been reported for 8-substituted-1-naphthoic acids.[6]

[6] K. Bowden and D. C. Parkin, *Can. J. Chem.* **47**, 185 (1969).

[7] The transmission coefficient[2a] is the ratio of the ρ values of −0.67 and −2.89 for the 4′-substituted-4-aminobiphenyls[4] and 3- and 4-substituted anilines,[8] respectively.

[8] A. I. Biggs and R. A. Robinson, *J. Chem. Soc.* 388 (1961).

[9a] S. K. Dayal, S. Ehrenson and R. W. Taft, *J. Am. Chem. Soc.* **94**, 9113 (1972); [b] P. R. Wells, S. E. Ehrenson and R. W. Taft, *Prog. Phys. Org. Chem.* **6**, 147 (1968); [c] S. Ehrenson, R. T. C. Brownlee and R. W. Taft, *Ibid.* **10**. 1 (1973).

[10] The dual substituent parameter equation relationship for the 4′-substituted-4-aminobiphenyls is $pK_a = 4.28 - 0.62\sigma_I - 0.55\sigma_R$,$R = 0.986$, $s = 0.065$ and for the 4′-substituted-3-aminobiphenyls is $pK_a = 4.35 - 0.66\sigma_I - 0.38\sigma_{R^-}$, $R = 0.907$, $s = 0.142$.

[11] The literature references and a description of the synthetic methods used for the preparation of these substituted aminobiphenyls can be obtained upon request to the corresponding author.

[12] J. P. Idoux and R. Zarrillo, *J. Org. Chem.* **40**, 1519 (1975).