for $CH_2{=}CHO^-$ plus $HCO_2CH{=}CH_2$. This is a reasonable size for a bimolecular exchange at a carbonyl group.[44]

For the proton-transfer part of the reaction coordinate, both the maximum and minima are highly delocalized structures. Solvation should not change their relative energies greatly, resulting in the maximum remaining so. It should be noted that the difference in enthalpy between the bottom of the second well and the proton-transfer maximum is comparable in size to E_{act} for such proton transfers in solution.[42] Such a solvation scheme could make proton transfer rate limiting as is often seen in solution.[2]

One of the most fundamental kinetic concepts in solution is that of the rate-limiting step. The overall rate of a reaction is controlled only by the free-energy difference between the highest energy transition state and the reactants. The nature of the reaction coordinate at all other points is irrelevant to the rate, though not to the nature of the product. In the gas phase, we have seen that this is not necessarily the case for the same reaction, however. The observed gas-phase rate is a function of the product of the efficiences across all the wells. This difference is ascribable to the different nature of the energetics involved. In the gas phase as in Figure 1, the reacting species are chemically activated to a energy greater than any of the "transition states" along the reaction coordinate. For this adiabatic reaction the rate is therefore not limited by any transition state but rather by the quantum properties of their excited states. Figure 2 resembles the solution-phase cases more in that a barrier above the adiabatic level exists. The rate is slowed, exactly as predicted by the usual solution-phase arguments, to less than 0.001 of collision rate, below the time window of the ICR. Thus solution-phase intuition does qualitatively work in ion–molecule reactions; it is only that there is such a narrow range between no barrier, as in Figure 1, and one sufficient to block any observable reaction, as in Figure 2, that it is rare to find cases where we know the energetics precisely enough to ascribe the observed rate to a true potential barrier and not to its manifestation in excited states. Figure 3 may represent such a case, but the estimated energetics are too uncertain to say for sure.

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The Relationship between Substituent-Induced Energy and Charge Effects in Proton-Transfer Equilibria

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Abstract: The relationship between substituent-induced changes in energy and in charge is investigated for various proton-transfer equilibria by using ab initio molecular orbital theory at the minimal basis STO-3G level. Linear relationships are found between the proton affinities of a variety of nitrogen, oxygen, and carbon bases and the electron populations of hydrogen atoms attached to the acidic center. Similar relationships are usually not followed by the charge on other atoms. These findings are interpreted by reference to calculations on model compounds.

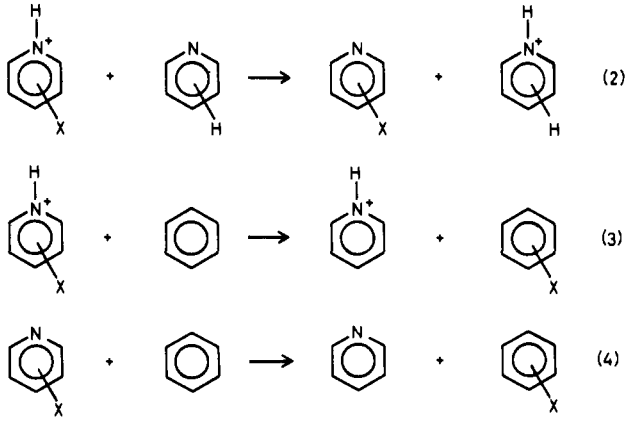
Introduction

(a) Energy Calculations. Ab initio molecular orbital calculations at the minimal basis set STO-3G level[1] have proven remarkably successful in the reproducing the experimental gas-phase energies for a variety of isodesmic proton-transfer reactions. For example, it has been shown[2] that theoretical energies for processes 1, de-

$$XCH_2NH_3^+ + HCH_2NH_2 \rightarrow XCH_2NH_2 + HCH_2NH_3^+ \quad (1)$$

scribing the effect of a β-substituent, X, on the proton affinity of methylamine, accurately parallel the measured reaction enthalpies for a wide range of substituents. Other examples include proton-transfer equilibria involving substitued quinuclidines,[3] phenols,[4] pyridines,[5] and anilines.[5]

Theoretical calculations also allow for partitioning of the substituent effect into components arising from each of the protonated and unprotonated forms. Thus, for example, the total effect of a substituent X on the proton affinity of pyridine (eq 2) may be broken down into its effect on the protonated molecule (i.e., eq 3) minus the corresponding effect on neutral pyridine (i.e. eq 4). Analyses of this type,[6] carried out on substituted pyridines,[5], anilines,[5] phenols,[4] and benzoic acids,[7] have shown that the effect of substituents on proton affinity arises primarily from interactions in the charged form.



(2)

(3)

(4)

(b) Charge Calculations. Ab initio calculations at the STO-3G level have also been used to obtain charge distributions according

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to the Mulliken[8] method, the resulting atomic electron populations following the general concepts of substituent effects. For example, the calculated[9] π-electron populations for monosubstituted benzenes clearly show the predominance of resonance effects at the ortho and para compared to the meta positions. Further, the total π-electron transfer between the substituent and the ring accurately parallels[10] the experimentally determined σ_R^0 values. The calculated populations also parallel[10] the relative carbon-13 chemical shifts at the meta and para carbon atoms. A similar relationship has been found[11] for the fluorine-19 shifts of a series of aryl-substituted β,β-difluorostyrenes.

(c) Energy–Charge Relations. Both the calculated relative energies and charges made for a series of related compounds thus seem meaningful. Implicit in the interpretation of fundamental energy changes in terms of the movement of charge is the assumption that the two quantities are directly related to one another. This assumption was specifically incorporated into the early theoretical treatment of aromatic acid dissociation energies by Roberts and Jaffe.[12] More recently, an empirical model of proton affinities has been postulated[13] which assumes a relationship between this quantity and the electrostatic potential at the proton. However, surprisingly little direct evidence is available on this point. Calculations at the INDO level have shown[14] that the charge on the carboxylic acid hydrogen[15] atom in substituted benzoic acids is approximately proportional to the pK_a values expressed as Hammett σ constants. Ab initio molecular orbital calculations at the STO-3G level have shown that the nitrogen inversion barrier in para-substituted phenols[16] parallel the extent of π-charge transfer between the ring and the NH_2 and OH groups, respectively. Rotational barriers in monosubstituted benzenes are proportional[17] to the charge-dependent intensities of certain infrared bands in the same molecule. By contrast, the total positive charge at the carbonium centers in certain alkyl cations increases[18] in the reverse order of decreasing stability (increasing hydride affinity).

Since our initial report[19] delineating a number of linear relationships between substituent effects on relative proton affinities and the corresponding protonic charges, several other comparisons have appeared in the literature. These include relationships (a) between the proton affinities of some alkyl chlorides[20] and the total charge on the chlorine and on the attached hydrogen atom in the protonated form (STO-3G), (b) between proton affinities and the charge on the acidic hydrogen atom for a series of substituted phenols and benzoic acids[21] (INDO), and (c) of aliphatic aldehydes[22] (STO-3G). There has also been considerable interest[23-25] in the relationship between proton affinities and core ionization energies, and recent publications[26] have related some gas-phase proton affinities to an electrostatic field model.

Table I. Ab Initio Molecular Orbital (STO-3G) Energies for Substituted Toluenes and Benzyl Cations (Hartrees)

	toluenes		benzyl cations	
subst	meta	para	meta	para
NH_2[b]	−320.788 66[a]	−320.787 40[a]	−319.969 29	−320.007 66
OMe	−378.880 49	−378.879 62	−378.055 84	−378.080 74
F	−363.933 55[a]	−363.932 89[a]	−363.101 42	−363.117 73
Me	−305.057 64	−305.057 35	−304.238 91	−304.246 35
H	−266.473 82[a]		−265.652 31	
CF_3	−597.438 54	−597.438 77	−596.606 47	−596.604 45
CN	−357.027 41[a]	−357.027 90[a]	−356.186 35	−356.186 66
CHO	−377.701 52	−377.701 78	−376.871 55	−376.872 81
NO_2	−467.167 51	−467.168 20	−466.319 27	−466.314 91

[a] Reference 6. [b] Planar C-NH_2.

Table II. Ab Initio Molecular Orbital (STO-3G) Calculations for Proton-Transfer Reactions of Substituted Ethylamines[a]

		cation			neutral	
subst	$\Delta E°$	Δq_H[b] (trans)	Δq_H[c] (cis)	Δq_N[d]	Δq_H[e]	Δq_N[f]
Et	2.1	−28	−16	0	−8	−10
Me	1.4	−21	−10	−1	−5	−9
$CHCH_2$	−0.5	−9	−2	1	17	13
CCH	−2.7	9	1	−5	21	23
NH_2	−2.5	−4	4	−3	11	0
OH	−2.8	35	5	−6	17	32
F	−6.4	53	21	−8	42	−14
CF_3	−6.4	37	19	5	34	47
CN	−11.3	66	30	−6	55	65
NO_2	−14.9	109	41	−13	67	93

[a] $\Delta E°$ in kcal mol^{-1} and Δq in 10^4 electrons (negative sign indicates increase in population). [b] $q_H = 0.6799$ in parent. [c] $q_H = 0.6802$ in parent. [d] $q_N = 7.3428$ in parent (cf. 7.0000 for neutrality). [e] $q_H = 0.8562$ in parent. [f] $q_N = 7.3795$ in parent.

Calculations

All calculations have been carried out at the STO-3G level[1] by using the Gaussian-77 series of computer programs.[27] The geometries used and calculated energies for the proton-exchange equilibria have already been described for the methylamines,[2] ethylamines,[2] quinuclidines,[3] pyridines,[5] hydrated pyridines,[28] anilines,[5] phenols,[4] benzyl anions,[29] benzenonium ions,[30] and some of the toluenes.[6] Standard geometries were used for the other toluenes and for the substituent[31] geometries in the benzyl cations. The carbon skeleton in the benzyl cations was the partially optimized structure found for the parent cation. The bond lengths were as follows: $C_\alpha C_1 = 1.3684$ Å; $C_1C_2 = 1.4406$ Å; $C_2C_3 = 1.3679$ Å; $C_1C_4 = 2.7698$ Å.

The CH_2 group was taken coplanar with the benzene ring, CH distance = 1.08 Å, and 120° angles. The calculated energies for these compounds are listed in Table I.

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Table III. Ab Initio Molecular Orbital (STO-3G) Calculations for Proton-Transfer Reactions of Substituted Methylamines and Quinuclidines[a]

	methylamines		quinuclidines	
subst	$\Delta E°$	Δq_H (NH_3^+)[b]	$\Delta E°$	Δq_H[c]
Et	4.9	−62		
Me	3.5	−54	0.9	−8
$CHCH_2$	3.2	−50		
CCH	−2.0	−7		
NH_2	0.2	−10	−1.5	3
OH	−2.5	39	−3.5	14
F	−9.0	43	−5.4	26
CF_3	−9.6	46		
CN	−15.9	76	−10.0	44
NO_2	−24.5	159	−13.9	76

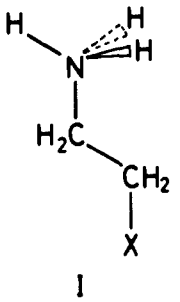
[a] $\Delta E°$ in kcal mol^{-1} and Δq in 10^4 electrons (negative sign indicates increase in population). [b] $q_H = 0.6743$ in parent. [c] $q_H = 0.7001$ in parent.

Results and Discussion

Aliphatic Compounds. Table II gives the calculated energies for the proton-transfer equilibria for substitued ethylamines.

$$XCH_2CH_2\overset{+}{N}H_3 + CH_3CH_2NH_2 \rightleftarrows XCH_2CH_2NH_2 + CH_3CH_2\overset{+}{N}H_3 \quad (5)$$

The geometry adopted[2] was the fully extended all trans form having NCCX coplanar. Table II lists the atomic electron



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populations on the acidic hydrogen atoms and for the nitrogen atom in both the acidic and neutral forms. A plot of the calculated energy for reaction 5 vs. the charge on the acidic protons, taken as the average of the cis and trans values, is linear. The least-squares slope is 2130 kcal mol^{-1} per electron, and the correlation coefficient (r) is 0.982. Similar plots can be obtained for the cis and trans protons taken separately, giving slopes of 3030 (r = 0.984) and 1230 (r = 0.967) kcal mol^{-1} per electron, respectively. A linear plot of slope 2230 kcal mol^{-1} per electron (r = 0.976) is also found between the calculated energy and the charge on the hydrogen atoms in the neutral form. There is only a small change with substituent in the population at the nitrogen atom in the cations (Table II) while the change in population at that atom in the neutral form shows only a rough relationship to the calculated energies for the equilibria.

Table III lists the corresponding results for substituted quinuclidines and methylamines. A good linear relationship, slope 1290 kcal mol^{-1} per electron (r = 0.992) was found between $\Delta E°$ and the charge on the acidic proton in the quinuclidinium ions but again the change in population at the nitrogen atom was small in the acidic form and that in the neutral form, only roughly related to the energies. A plot[19] of $\Delta E°$ for reaction 1 vs. the charge on the acidic hydrogens for methylammonium ions has slope 1360 kcal mol^{-1} per electron (r = 0.969).

It has been reported[20] that the total charge on the acidic hydrogen and chlorine atoms in some protonated ethyl chlorides is linearly related to the calculated (STO-3G) proton affinities of the halides. We find that a plot of the PA vs. the charge on the acidic hydrogen alone is linear with slope 450 kcal mol^{-1} per electron. We have also examined the relationship[22] between calculated PA and the charge on the acidic hydrogen for aliphatic aldehydes. Here STO-3G calculations for both standard and optimized geometries give reasonable linear plots of slope approximately 800 kcal mol^{-1} per electron for the trans forms; the points show more scatter for the cis forms and the slope is lower (ca. 540 kcal mol^{-1} per electron). Similar energy–charge relationships have also been found[32] for a series of substituted acetic and propionic acids having slopes of 1610 and 1875 kcal mol^{-1} per electron, respectively.

Table IV. Ab Initio Molecular Orbital (STO-3G) Calculations for Equilibria Involving Substituted Pyridines[a]

		cations		neutral	hydrates	
subst	$\Delta E°$[f]	Δq_H[b]	Δq_N[c]	Δq_N[d]	$\Delta E°$	Δq_H
3-NH_2[e]	3.5	−18	102	117		
4-NH_2[e]	16.1	−142	−246	−262		
3-OMe	−0.3	−17	79	105		
4-OMe	9.3	−76	−196	−171	6.0	−43
3-F	−6.3	51	76	125	−4.4	33
4-F	−0.2	−10	−79	−70	−0.3	4
3-Me	2.5	−27	16	15		
4-Me	5.0	−49	−71	−65	3.3	−22
3-CF_3	−6.8	37	30	58		
4-CF_3	−6.8	34	23	92	−5.1	22
3-CN	−12.4	73	32	84	−9.1	43
4-CN	−11.4	51	39	157	−8.6	35
3-CHO	−3.6	13	15	6		
4-CHO	−2.9	−3	−11	75		
3-NO_2	−17.4	115	−9	109		
4-NO_2	−16.7	97	35	230		

[a] $\Delta E°$ in kcal mol^{-1} and Δq in 10^4 electrons (negative sign indicates increase in population). [b] $q_H = 0.6891$ in parent. [c] $q_H = 7.2464$ in parent (cf. 7.0000 for neutrality). [d] $q_N = 7.2415$ in parent. [e] Planar CNH_2. [f] Reference 5.

Thus, linear energy–charge relationships apparently are found for each case so far investigated for proton-transfer reactions of a variety of aliphatic systems. For related systems, such as the proton affinity of amines, the slopes become greater with increasing distance of the substituent to the charged site and are sensitive to the particular geometry involved.

Aromatic Compounds. Table IV lists the relevant ab initio results for 3- and 4-substituted pyridinium ions. A plot of $\Delta E°$ vs. the charge on the acidic proton is bilinear with slopes 1110 and 1700 kcal mol^{-1} per electron for resonance donating and accepting substituents, respectively, although a linear plot, slope of 1360 kcal mol^{-1} per electron, can also be drawn (r = 0.988). No satisfactory relationship is found between $\Delta E°$ and the total charge on the nitrogen atom in the acidic form. There is, however,[24] a rough proportionality between the energy and the charge on the nitrogen in the neutral pyridines. The ab initio calculation (Table IV) suggests that, in contrast to the formal charge picture, protonation of pyridine hardly affects the charge at nitrogen. We have also examined the relationship between $\Delta E°$ and the various orbital electron populations at the nitrogen atom. The only approximate relationship found was with the $2p_z$ density (in direction of NH axis) at the nitrogen atom in the acidic form.

Table IV also lists the corresponding figures for the equilibria including one molecule of water.

$$XC_5H_4\overset{+}{N}H\cdot H_2O + C_5H_5N\cdot H_2O \rightleftharpoons XC_5H_4N\cdot H_2O + C_5H_5\overset{+}{N}H\cdot H_2O \quad (6)$$

It is already been shown[2,33] that a linear energy–charge plot may be obtained between $\Delta E°$ and the charge on the acidic proton for reaction 6 and that the energy of hydration of the charged form also follows the acid proton density. Similarly the difference in energy between equilibria 6 and that for the unhydrated species (equilibria 2) follows the charge values of the protons of the unhydrated pyridinium ions.

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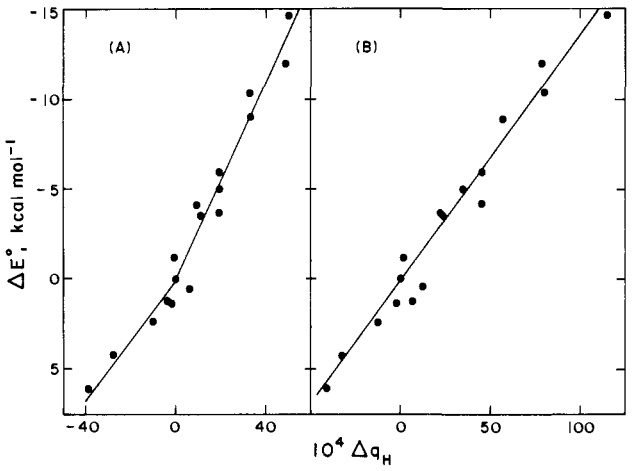


Figure 1. Plot of calculated proton affinities, $\Delta E°$, of substituted anilines vs. the charge on the proton, Δq_H, (A) in acidic form (B) in neutral form.

Table V. Ab Initio Molecular Orbital (STO-3G) Calculations for Equilibria Involving Substituted Anilines[a]

		anilinium ions		anilides	
subst	Δq_H[b] (NH_2)	$\Delta E°$[c]	Δq_H[d] (NH_3^+)	$\Delta E°$[e]	Δq_H[b] (NH^-)
3-NH_2	6	1.2	−4	−0.1	7
4-NH_2	−41	6.1	−39	−4.8	−35
3-OMe	10	0.6	6	2.2	21
4-OMe	−32	4.2	−28	−2.9	−25
3-F	23	−3.8	19	5.0	41
4-F	−1	−1.1	−1	1.3	−3
3-Me	−3	1.3	−3	−0.3	5
4-Me	−12	2.4	−10	−1.0	−1
3-CF_3	34	−5.0	19	7.6	59
4-CF_3	45	−5.9	19	10.7	96
3-CN	57	−9.0	33	13.4	97
4-CN	81	−10.4	33	20.2	186
3-CHO[g]	24	−3.6	11	5.7	41
4-CHO	45	−4.2	9	13.3	158
3-NO_2	78	−12.0	49	16.9	131
4-NO_2	114	−14.8	50	27.7	269

[a] $\Delta E°$ in kcal mol^{-1} and Δq in 10^4 electrons (negative sign indicates increase in population). [b] q_H in parent, 0.8185. [c] $\Delta E°$ from ref 5. [d] q_H in parent, 0.6689. [e] $\Delta E°$ from ref 29. [f] q_H in parent, 0.9762. [g] Not included in energy-charge plots since lowest energy conformation of CHO changes between neutral and acidic form.

The results of STO-3G calculations for two possible proton-transfer equilibria with substituted anilines, eq 7 and 8, are given in Table V. Figure 1 shows plots of $\Delta E°$ for equilibria 7 against

$$XC_6H_4\overset{+}{N}H_3 + C_6H_5NH_2 \rightleftharpoons XC_6H_4NH_2 + C_6H_5NH_3^+ \quad (7)$$

$$X_6H_4NH^- + C_6H_5NH_2 \rightleftharpoons XC_6H_4NH_2 + C_6H_5NH^- \quad (8)$$

the charge on hydrogen (attached to nitrogen) in the acidic and neutral forms. It is seen that the plot is bilinear for the charge on the acidic form but linear (slope of 1400, kcal mol^{-1} per electron, $r = 0.983$) for that on the neutral molecules. A similar situation exists for the reaction 8 but here the plot of $\Delta E°$ against the hdyrogen electron population is bilinear for the neutral form and linear (slope of 1060, kcal mol^{-1} per electron, $r = 0.984$) for the anilides. Thus, linear plots seem to result in these aromatic systems for cases where the form used as the basis for the charge differences is also that having the dominant substituent resonance interactions.

The theoretical results for equilibria involving substituted phenols are given in Table VI.

$$XC_6H_4O^- + C_6H_5OH \rightleftharpoons XC_6H_4OH + C_6H_5O^- \quad (9)$$

A plot of ΔE for reaction 9 vs. the charge on the acidic proton for the phenols is bilinear as found for the corresponding plot for

Table VI. Ab Initio Molecular Orbital (STO-3G) Results for Substituted Phenols and Phenoxides[a]

		phenols			phenoxides
subst	$\Delta E°$[b]	Δq_H[c]	Δq_O[d]	$-q_O^{e-}$ ($2p_x$)	Δq_O[f]
3-NH_2	−0.1	9	0		19
4-NH_2	−4.9	−42	−39	38	−81
3-OMe	2.1	18	18	−14	36
4-OMe	−3.0	−33	−29	31	−62
3-F	5.4	31	34	−24	77
4-F	1.6	−1	0	4	−14
3-Me	−0.4	−4	−5	1	10
4-Me	−1.0	−15	−13	13	1
3-CF_3	8.4	34	32		116
4-CF_3	11.5	42	42	−34	207
3-CN	14.5	56	54	−41	183
4-CN	21.4	75	75	−60	402
3-CHO	5.9	15	15	−9	65
4-CHO	13.8	41	39	−35	350
3-NO_2	18.1	86	72	−65	233
4-NO_2	29.2	105	106	−85	594

[a] $\Delta E°$ in kcal mol^{-1} and Δq in 10^4 electrons (negative sign indicates increase in population). [b] Reference 4. [c] q_H in phenol, 0.7837. [d] q_O in phenol, 8.2993 (cf. 8.0000 for neutrality). [e] $q_O(2p_x)$, 1.3769. [f] q_O in phenoxide, 8.4727.

Table VII. Ab Initio Molecular Orbital (STO-3G) Results for Substituted Toluenes, Benzyl Cations, and Benzyl Anions[a]

	cations		anions		neutrals
subst	$\Delta E°$	Δq_H[b] (CH_2^+)	$\Delta E°$[c]	Δq_H[d,e] (CH_2^-)	Δq_H[b] (CH_3)
3-NH_2	1.3	−28	0.6	−8	−1
4-NH_2	26.2	−187	−6.3	−60	−31
3-OMe	−2.0	18	2.8	30	12
4-OMe	14.2	−112	−4.2	−17	−23
3-F	−6.7	43	5.4	33	22
4-F	4.0	−22	0.6	1	−1
3-Me	1.7	−9	−0.1	4	
4-Me	6.6	−45	−1.3	3	
3-CF_3	−6.6	33	8.1	55	25
4-CF_3	−7.9	30	12.1	88	28
3-CN	−12.3	71	13.9	94	
4-CN	−12.4	49	23.0	171	50
3-CHO	−5.3	23	5.6	37	17
4-CHO	−4.7	−12	15.3	146	24
3-NO_2	−16.8	94	17.3	122	58
4-NO_2	−19.9	89	31.9	251	70

[a] $\Delta E°$ in kcal mol^{-1} and Δq in 10^4 electrons (negative sign indicates increase in population). [b] q_H in parent, 0.8438. [c] Reference 29. [d] q_H in parent, 1.0456. [e] Reference 34. [f] q_H in parent, 0.9341.

aniline acidities (eq 8). The dependence of ΔE on the total charge on the oxygen atoms was examined both for the phenoxides and the phenols; the former relationship was linear, the latter bilinear. Both showed considerable scatter. An examination of the orbital electron populations at the oxygen atom in the phenols showed that the only linear relationship was that for the $2p_x$ orbital with either $\Delta E°$ or, alternatively, with the change in population at the attached hydrogen. The $2p_x$ orbital is at right angles to the line of the CO axis and in the plane of the benzene ring. Clearly linear energy–charge relationships are accurately followed only for the acidic hdyrogens or for orbitals, at attached atoms, that are not involved in bonding to the other atoms in the system.

Two proton-transfer equilibria are also possible with substituted toluenes, the relevant results being given in Table VII.

$$XC_6H_4\overset{+}{C}H_2 + C_6H_5CH_3 \rightleftharpoons XC_6H_4CH_3 + C_6H_5\overset{+}{C}H_2 \quad (10)$$

$$XC_6H_4\bar{C}H_2 + C_6H_5CH_3 \rightleftharpoons XC_6H_4CH_3 + C_6H_5\bar{C}H_2 \quad (11)$$

Figure 2 shows plots of $\Delta E°$ for process 10 against the charge on the hydrogen atoms on the toluene methyl group or carbonium

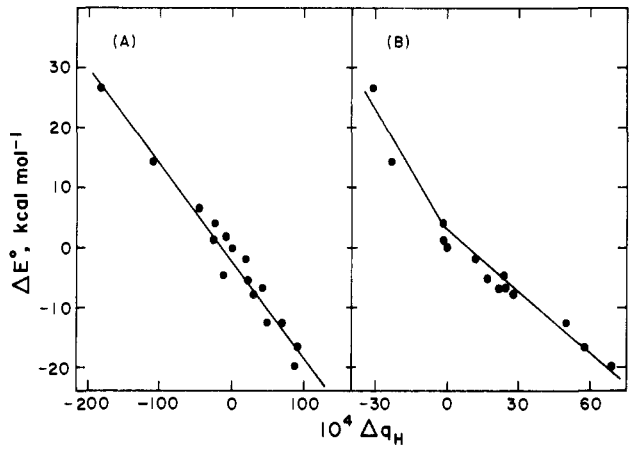


Figure 2. Plot of calculated hydride affinities of substituted benzyl cations, $\Delta E°$, vs. the charge on the proton, Δq_H, (A) in the benzyl cation and (B) in the neutral form.

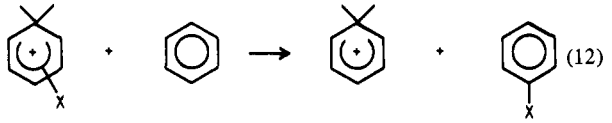
Table VIII. Ab Initio Molecular Orbital (STO-3G) Results for Substituted Benzenes and Benzeneonium Ions[a]

	para		meta	
subst	$\Delta E°$ [b]	Δq_H [c]	$\Delta E°$ [b]	Δq_H
NH_2	27.2	−37	0.6	11
OH	16.0	−31	−5.3	21
F	3.7	7	−7.5	53
Me	8.5	−22	2.0	−11
CF_3	−8.4	60	−7.5	57
CN	−13.8	105	−14.0	100
NO_2	−22.1	147	−17.9	141

[a] $\Delta E°$ in kcal mol^{-1} and Δq_H for hydrogen at meta or para position in monosubstituted benzenes in 10^4 electrons (negative sign indicates increase in population). [b] Reference 30. [c] q_H in parent, 0.9371.

CH_2 center, respectively. Similar plots are obtained for reaction 11. The plots are analogous to those found for equilibria 7 and 8; they are linear for the charge on the charged forms where resonance is important and bilinear for the charge on the neutral form. The slopes of the linear plots are 1570 kcal mol^{-1} per electron (r = 0.981) for equilibria 10 and 1270 kcal mol^{-1} per electron (r = 0.989) for equilibria 11.

Table VIII lists the STO-3G results for equilibria 12. The


(12)

$\Delta E°$ values were earlier shown[30] to be proportional to the σ^+ values of the substituents. A plot of $\Delta E°$ vs. the charge on the hydrogen atom on the neutral benzene derivative gives a reasonable bilinear relationship in spite of the very significant structural change involved in the equilibria. The slopes are approximately 6000 and 1400 kcal mol^{-1} per electron for the resonance-donating and -withdrawing substituents, respectively.

A linear energy–charge relationship has also been shown[19,35] to exist for the proton-transfer reaction of benzoic acids between $\Delta E°$ and the charge on the carboxyl hydrogen atom. The slope is approximately 1800 kcal mol^{-1} per electron.

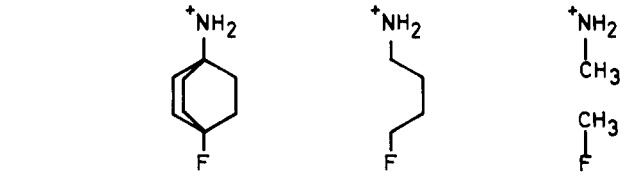
Interaction Energies in Charged and Neutral Forms. It is interesting that the energy–charge relationships extend to the proton affinities of substituted methylamines since here considerable substituent effects occur in the neutral form via hyperconjugation. A major dependence on substituent interaction energies in the charged form has been shown for the proton-transfer equilibria of aromatic systems such as phenols,[4] anilines,[5] pyridnes,[5] and carboxylic acids.[35] This is also the case for quinuclidines and

(35) Mezey, P. G.; Reynolds, W. F. *Can. J. Chem.* **1977**, *55*, 1567.

Table IX. Interaction Energies (STO-3G) for Substituted Ethylamines and Methylamines (ΔE in kcal mol^{-1})

	ethylamine			methylamine		
		ΔE_{int}			ΔE_{int}	
	$\Delta E°$	cation	neutral	$\Delta E°$	cation	neutral
Et	2.1			4.9	7.2	2.3
Me	1.4	1.4	0.0	3.5	5.7	2.2
NH_2	−2.5	−3.3	−0.8	0.2	5.7	5.6
OH	−2.8	−3.7	−0.9	−2.5	5.1	7.6
F	−6.4	−7.6	−1.2	−9.1	0.1	9.1
CN	−11.3	−12.0	−0.8	−15.9	−15.6	0.3

Chart I

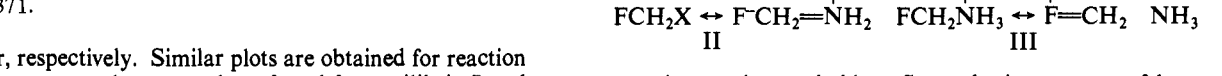


IV V VI

ethylamines. Table IX gives the relevant data for substituted ethylamines and methylamines. It is obvious that while substituent energy effects are small in the neutral forms of β-substituted ethylamines, there are substantial effects in a neutral methylamines as evidenced by the theoretical energies for reaction 13. This

$$XCH_2NH_2 + CH_4 \rightleftharpoons XCH_3 + CH_3NH_2 \qquad (13)$$

hyperconjugative effect can be represented by canonical forms II. The very small interaction energy in the fluoromethyl-



ammonium cation probably reflects the importance of hyperconjugation as shown in III compensating for destabilizing electrostatic interactions.

Energy–Charge Relationships. To summarize our empirical findings, it appears that energy–charge relationships exist between proton affinities and the charge on hydrogens attached to the reaction center over a wide range of proton-transfer reactions involving nitrogen, oxygen, and carbon bases. Similar relationships do not usually exist or are much less pronounced for the nitrogen or oxygen atoms. The energy–charge relationships have proportionality constants within a factor of 10 and seem to be larger for systems where the substituent is further from the reaction site. The proportionality constants also clearly vary with the angle subtended by the substituent to the reaction site.

In order to further investigate this dependence of energy–charge relationships on structure, one would like to have substituent-induced charge and energy values for a wide variety of systems of differing geometries. Unfortunately, a sufficient number of such systems is restricted by the constraints of molecular geometry and by computational restrictions on the number of orbitals involved. However, it has recently been shown[36,37] that the relative proton affinites of aliphatic amines are well approximated by using an isolated molecule approach. In this, an isodesmic proton-exchange equilibria is used as above, but the amine $XC_xH_yNH_2$ is replaced by the two molecules XCH_3 and CH_3NH_2 with corresponding atoms at the same relative geometries as the alkylamine. The appropriate isodesmic process is thus as shown in eq 14. The

$$CH_3\overset{+}{N}/CH_3X + CH_3NH_2/CH_4 \rightleftharpoons CH_3\overset{+}{N}H_3/CH_4 + CH_3NH_2/CH_3X \qquad (14)$$

(36) Topsom, R. D. *Tetrahedron Lett.* **1980**, 403.
(37) Topsom, R. D. *J. Am. Chem. Soc.* **1981**, *103*, 39.

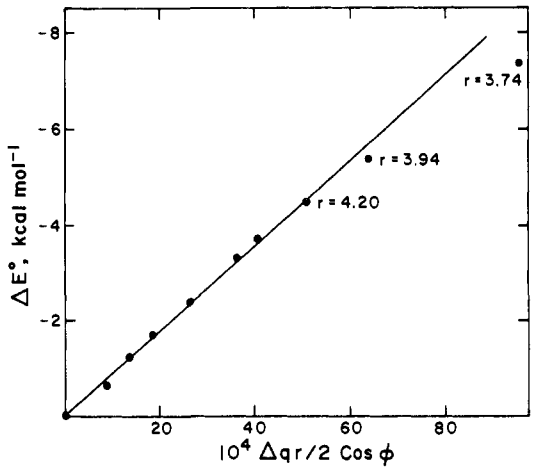


Figure 3. Plot of calculated proton affinities of NH_2CH_3/CH_3F vs. $\Delta qr/2 \cos \phi$.

proton affinities calculated for the amines in Chart I show the level of agreement obtained. It would appear, therefore, that the isolated molecule approach offers a computationally simple method to investigate the effect of geometry variations on ΔE and on $\Delta q_H(NH_3^+)$.

It has been shown[36] that for a linear arrangement of the heavy atoms as in VI, the $\Delta E°$ values are proportional to $1/r^2$, the inverse square of the distance r between the midpoint of the CF bond and the calculated center of charge in the $CH_3NH_3^+$ molecule. This identity is in accord with simple electrostatic theory which gives eq 15 since for linear arrangements $\cos \theta = 1$, where θ is the angle

$$E \propto \frac{\mu \cos \theta}{r^2} \tag{15}$$

subtended at the CF bond by a line drawn to the center of charge. It has also been shown[37] that $\Delta E°$ varies as $\cos \theta$ for isolated molecule calculations, where r is kept constant.

The relationship[38] for the electric field of a dipole acting along an isolated bond is

$$E_{bond} = \frac{\mu(2 \cos \theta \cos \phi - \sin \theta \sin \phi)}{r^3} \tag{16}$$

where ϕ is the angle subtended at the polarized bond (in this case an NH bond in $CH_3^+NH_3$) by the line drawn to the midpoint of CF bond. Thus the charge induced by polarization should follow $1/r^3$ rather than $1/r^2$ (eq 15), and further the relative geometry of the NH bond is important unlike the situation with energy values. These are major reasons why the proportionality constant between energy and charge changes from one series to another. For a linear arrangement as in VI, eq 16 reduces to $E = 2\mu \cos \phi/r^3$ and thus a plot of ΔE vs. $\Delta qr/2 \cos \phi$ should be linear. This is illustrated in Figure 3 (using calculations from ref 37). The plot is linear for values of r greater than 4 Å, corresponding to an intermolecular hydrogen–hydrogen distance of less than the sum of the van der Waals radii. Provided $\cos \phi$ does not change greatly, we therefore anticipate that the energy–charge proportionality constants will increase as r increases. This is in accord with figures found above, for example, for anilines compared to pyridines or for ethylamines compared to methylamines. Changes in Δq_H with angle are not always well described by eq 16 where $\cos \theta \neq 1$ since such values seem sensitive to the polarization of other parts of the molecule.[37] Thus we cannot predict exactly the expected field effects on energy–charge relationships.

Conclusions

It has been shown that linear energy–charge relationships exist for proton-transfer equilibria involving a wide variety of nitrogen, oxygen, and carbon acids and bases. These relationships generally only pertain to the charge on hydrogen atoms attached to the center involved in the proton transfer. This limitation seems to arise because the charges on other atoms are affected by complex multiorbital interactions with the rest of the molecule as the substituent changes. The linear energy–protonic charge relationships found for the aliphatic systems exist because both the energy and the charge depend on the magnitude of the substituent dipole. Changes in energy–charge ratios can be understood in terms of the differing variation of energy and of charge with the geometric relationship of the substituent to the reaction center and the XH bond. We can therefore broadly anticipate the changing energy–charge ratios between different series of molecules. These conclusions are in agreement with an earlier suggestion[35] that the parallel changes between effects on energy and on charge result from predominant field effects on both rather than resulting from a cause–effect relationship.

The situation with the equilibria of aromatic derivatives is complicated by resonance interactions. If the charge difference taken refers to the form, either protonated or unprotonated, having the dominant substituent resonance interactins, then linear relations are still observed. Energy–charge relationships based on the other form tend to be bilinear. It must be noted that the relationships are not precise, reflecting, at least in part, the differing geometrical dependences of energy and charge effects.

Acknowledgment. This material is based upon work supported by the National Science Foundation under Grant CHE-7823115.

(38) Adcock, W.; Khor, T.-C. *J. Am. Chem. Soc.* **1978**, *100*, 7799.