

Molecular Orbital Studies of Organic Substituent Effects. Semiempirical Calculations on Charge and Energy Perturbation through the Benzene Nucleus in a Model S_N2 Reaction

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Abstract: Semiempirical molecular orbital calculations on a model S_N2 exchange reaction (of substituted benzyl chlorides with chloride ion) are used to investigate the electronic origins of substituent effects in the reactions of benzene derivatives. CNDO/2 calculated substituent effects on activation energy are correlated with the substituent constants of the Hammett–Burkhardt linear free energy relationship and discussed in terms of mutual energy and charge perturbation of substituent, molecular framework, and reaction site. Electron density perturbation of reaction site and ring and of substituent and ring were found to be essentially independent of one another in this system. Energetic response to substitution was much larger in the (anionic) transition states than in the (neutral) benzyl chlorides.

The mental dissection of a reacting molecule into reaction site, skeleton, and substituents, each somewhat independent of the others and having its own consistent properties, has allowed the organic chemist to bring order to his consideration of the myriad reactions which nature and his synthetic imagination have presented for study. The like response of similar reactive systems to similar changes in these molecular building blocks is the foundation upon which the considerable predictive power of physical organic chemistry rests; it is in terms of interactions between these building blocks that the specific reactivity of a specific molecular system can be predicted or explained.

The new language of electronic structure theory was adopted wholeheartedly by many of those who sought to understand and quantify these interactions; it provided a useful and suggestive framework for their empiricism. Classic work in this area,¹ much of it from the English school led by Lapworth, Robinson, and Ingold, identified four modes of interaction which, acting in a static manner within reactants and products before and after reaction or in a dynamic manner as reactants proceed through transition states to products during the course of a reaction, are usually decisive in determining the equilibrium or rate constant for a given chemical process. Two of these, the field effect and the steric effect, are transmitted through space. They are pairwise interactions which do not depend upon the detailed electronic nature of some third part of the molecule for their transmission. The other two, the inductive effect and the conjugative effect, are quite different. These quasi-pairwise interactions travel *through* a third component of the molecule and depend in a profound way upon its electronic structure.

Regardless of the detailed mechanism of interaction, Hammett^{2,4} and Burkhardt³ noted that in one large class of reactive systems, those in which the molecular framework is a benzene ring and substituent and reactive side chain are in meta or para relation to one another, there are broadly applicable *quantitative* relationships between substituent effects on different reactions within the class. Though it was recognized quite early that these relationships imply direct proportionality between free energy effects of substitution in each of the correlated processes,⁵ there is no thermodynamic necessity for this linearity, Hammett originally emphasized² and has recently reemphasized⁶ the purely empirical origin of his and Burkhardt's correlation equation and the necessity for great care in interpreting it. Despite this, unsupported assertions of relationships between Hammett parameters and

electron densities are not uncommon. Such hypotheses may be consistent with the equation but are not in any direct way consequences of it; the parameters are *energetic* quantities which are related to electronic structural effects only by some theory of the latter.

The English school's qualitative electronic effect theory of organic reactivity has inspired several extensions of the Hammett–Burkhardt formulation. The most interesting of these attempt at least a qualitative assessment of the relative contributions of various factors to the observed substituent effects.^{7–12} Unfortunately, none of these attempts is unambiguously successful. As Exner has emphasized,¹³ the “mesomeric”, “resonance”, or “conjugative” terms used in the various treatments “have no immediate relation with the so-called theory of resonance”, but reflect either the difference between constants for particular classes of reactions,^{7,12} which are themselves complex quantities, or the difference between properties of conjugated and nonconjugated systems^{9,10} which differ in many respects besides that of favorable π orbital overlap (which can in any event allow π inductive as well as mesomeric interactions).

This may be inevitable. It is certainly physically meaningful to distinguish between π and σ electrons (at least at a high level of approximation) in substituted benzene systems; a dissection of their substituent effects into π and σ components *should* be possible. And it is certainly useful to imagine models of the unperturbed reaction site, skeleton, and substituent and mentally allow them to interact as an aid to predicting and understanding the final electron distribution. But different models (e.g., the valence bond based English school model and the molecular orbital model), each of which may be quite adequate to describe the system of interest, use quite different *pictures* of the electron distribution; these different pictures, equivalent when applied in toto, may nevertheless *partition* identical net changes in electron distribution differently. This presents no problem when observables are calculated from complete versions of either model, but becomes one when only certain terms are evaluated: care must be taken that *all* important terms have been retained. At least as much care must be exercised when, conversely, total observed effects are attributed to some subset of the terms in a model.

In particular, though the English school's separate consideration of them may have predictive value in some circumstances, the conjugative effect and the π component of the inductive effect can have quite similar consequences: displacement of electrons within the π system. Especially when

Table I. Summary of Calculations on S_N2 Halogen Exchange Reactions Y⁻ + CH₃X → YCH₃ + X⁻

	$E_T(\text{YCH}_3\text{X}^-)^a$	$E_T(\text{CH}_3\text{X}^-)^a$	$E_T(\text{Y}^-)^a$	$\Delta E^{\#b}$	r_{CX}^{0c}	$\Delta r_{\text{CX}}^{\#d}$	r_{CH}^{0c}	$\Delta r_{\text{CH}}^{\#d}$	Method	Ref
Y = F; X = F										
Nonempirical										
BDV-69	-238.4639	-139.0342	-99.4160	-8.6	1.42	+0.4578	1.08	-0.02	SCF	27
DV-70	-238.5150	-139.0805	-99.4471	+7.9	<i>e</i>	<i>e</i>	<i>e</i>	<i>e</i>	SCF	28a
DB-71	-238.5406	-139.0978	-99.4542	+7.2	1.4022	+0.4956	1.0788	-0.0180	SCF	29a
DVR-74	-238.7814	-238.7719 ^f		+5.9	<i>e</i>	<i>e</i>	<i>e</i>	<i>e</i>	CI	30
B-75	-238.5207	-139.0707	-99.4534	+2.1	1.438	+0.3847	1.088	-0.016	SCF	31
KA-76	-238.9647	-139.3765	-99.6023	+8.8	1.40	+0.39	1.08	<i>e</i>	CEPA-PNO ^g	32
Semiempirical										
CGS-72	-64.7244	-37.0996	-27.4841	-88.3	1.344	+0.095	1.119	+0.039	CNDO/2	33
SH-73	-64.0969				1.354	+0.10	1.121		CNDO/2	34
D-76				<-50	1.351	+0.112			INDO	36
Y = Cl; X = Cl										
Nonempirical										
KA-76	-958.7755	-499.2527	-459.5382	+9.7	1.78	+0.61	1.110	-0.05	CEPA-PNO ^g	32
Semiempirical										
H-72	-41.3384	-15.866		<0	1.685	+0.13	1.115		CNDO/2	<i>h</i>
This work ⁱ	-87.4047	-71.2182	-16.1039	-51.84	1.781	+0.225	1.110	-0.008	CNDO/2	
Y = F; X = Cl										
Nonempirical										
KA-76	-598.3671	-498.9417	-99.4014	-15.06 ^j	1.78	+0.29	1.110	-0.05	SCF	32
Y = Cl, X = Br										
Semiempirical										
BZ-74									EHT	<i>k</i>

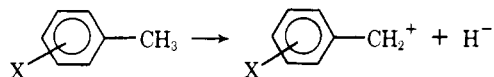
^a Hartrees. ^b kcal/mol (conversion factors: 1 Hartree = 627.503 kcal/mol = 27.2107 eV). ^c CH₃X bond length, Ångstroms. ^d The difference $r(\text{CH}_3\text{XY}^-) - r(\text{CH}_3\text{X})$, Ångstroms. ^e Taken from ref 27. ^f Coupled electron pair approximation with pair natural orbitals. Said to be a good approximation to a large-scale CI calculation; see R. Ahlrichs, H. Lischka, V. Staemmler, and W. Kutzelnigg, *J. Chem. Phys.*, **62**, 1225 (1975). ^g $E_T(\text{CH}_3\text{F}) + E_T(\text{F}^-)$. ^h G. M. Hallman, Ph.D. thesis, University of Toronto, 1972. ⁱ The skeleton is C₆H₅CH₂⁻ rather than CH₃⁻. Additional geometric parameters, of interest in this lower symmetry system, are $\theta_{\text{CCCl}}^0 = 113.7^\circ$, $\Delta\theta_{\text{CCCl}}^{\#} = -17.3^\circ$; $\theta_{\text{HCH}}^0 = 105.3^\circ$, $\Delta\theta_{\text{HCH}}^{\#} = 10.7^\circ$; $\phi_{\text{CH}_2 \text{ plane, ring plane}}^0 = 45.5^\circ$, $\Delta\phi^{\#} = -45.5^\circ$. ^j According to ref 32, FCH₃Cl⁻ is a true saddle point, preceded on the reaction coordinate by an ion-dipole complex of lower total energy. ^k L. Bobkiewicz and B. Zurawski, *Bull. Acad. Pol. Sci., Ser. Chem.*, **22**, 457 (1974).

it is recalled (vide supra) that the Hammett constants reflect energy changes rather than electron density changes per se, attempts to identify just one of these with an independent term in a correlation equation does not seem to follow from the nature of the experimental data. Dissection of parameters into "inductive" and "resonance" terms has, however, been useful in comparing the trends of "normal" behavior in different systems.

Molecular Orbital Models

Semiempirical π molecular orbital theory can model some aspects of substituent effect transmission through the benzene ring and it has been used for that purpose often. Jaffe's earliest work¹⁴ used a highly simplified model of the π transmission process and assumed a direct proportionality between π charge changes and total energy changes as reflected in ρ 's and σ 's. This work calibrated the π electron theory so it could be used for energy calculations in studies of modified σ 's for reactions with special electronic demand^{15a} and of the separation of inductive and mesomeric effects^{15b,c} (redefined, in effect, as σ and total π effects). Almost simultaneously,¹⁶ Sixma developed a simple procedure for calculating σ 's which included an electrostatic field term and an explicit (though crude) calculation of activation energy.

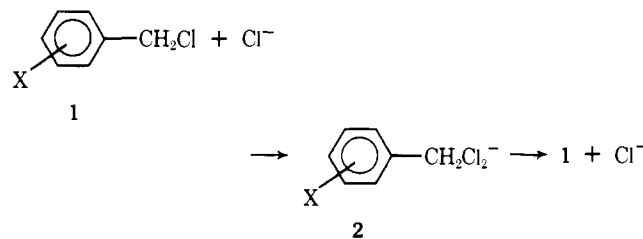
All-valence-electron models should allow a more complete examination of substituent effect transmission. Streitwieser and Jesaitis¹⁷ used such a method in investigating the system



(similar to Sixma's model) in a series of semiempirical SCF calculations; the resulting "activation energies" correlate rather well with rate data for S_N1 solvolysis reactions. (Interestingly, calculated charge density at the highly electrophilic reaction site bears a simple relation to calculated total en-

ergy—and experimental rate of reaction—only when the substituent significantly *enhances* charge donation to that site. The source of the extra electron density is not indicated.)

In the present paper, we report a series of CNDO/2 calculations¹⁸ on a model for the S_N2 displacement reactions of substituted benzyl halides. The model takes the substituted benzyl chloride **1** as starting material and the substituted anion **2** as a model for the transition state:



The reaction site in this system ought to interact with benzene ring and substituent differently than the S_N1 reaction site studied by Streitwieser and Jesaitis does; in particular, the reaction site and substituent should produce more nearly equal perturbations in the benzene skeleton than they do in the arylmethyl cations. Examination of this system, with its anionic transition state, should provide complementary data for a general attempt to understand substituent effect transmission in benzene derivatives.

Semiempirical calculations are most likely to prove useful when they can be compared with related experimental and high-quality nonempirical electronic structural data, and when a body of experience has accumulated from comparable calculations on related systems. Since our computations deal with isolated molecules, the most appropriate experimental data would be derived from studies of gas-phase nucleophilic displacement reactions. Such data have begun to appear,¹⁹⁻²¹ but do not yet include rate data for series of similar but variously

Table II. Calculated and Experimental Dipole Moments (D)

Molecule	MINDO/3	CNDO/2	Expt ^a
C ₆ H ₅ CH ₃	2.23	0.11	0.37
C ₆ H ₅ CH ₂ F		1.79 ^b	1.77 ^c
C ₆ H ₅ CH ₂ Cl	2.37	1.87	1.84 ^c
C ₆ H ₅ CF ₃	4.30	2.88	2.86
C ₆ H ₅ NO ₂	5.16	4.75	4.28

^a A. L. McClellan, "Tables of Experimental Dipole Moments", W. H. Freeman, San Francisco, Calif., 1963. ^b At optimized CNDO/2 geometry; others at MINDO/3 geometries. ^c Solution data; others from gas-phase experiments.

substituted compounds. Because it has been argued that internal energy changes (which are what we calculate) should be approximately proportional to the Hammett equation free-energy parameters,²² we have used σ constants as one basis for comparison with experiment; rate data²³ from the reaction of substituted benzyl chlorides with iodide ion in acetone, a relatively nonpolar solvent, indicate that the σ 's defined by benzoic acid ionization equilibria are the appropriate ones.

There have been several high-quality nonempirical studies of the S_N2 exchange reaction of methyl fluoride with fluoride ion;²⁵⁻³⁰ one of these³⁰ also considered the corresponding chloride exchange and the mixed halogen displacement. CNDO/2 studies of the methyl fluoride exchange reaction have also been carried out,^{31,32} as has an INDO³³ study of that and several related reactions.³⁴ Pertinent results from these papers are gathered in Table I.

We have chosen to use CNDO/2 for charge and energy calculations in this work because (1) the low cost of these calculations allows us to examine large, moderately realistic reactive systems; (2) a large body of experience of the method's strengths, weaknesses, and limitations is available;^{17,35} (3) its parameters were chosen to produce reasonable charge distributions²¹ (vide infra); and (4) the method has already been applied with some success to the related benzyl cation system.^{17a} Modified versions of Dobosh's CNINDO program³⁶ were used for all calculations.

The CNDO/2 method was not designed to reproduce experimental geometries, nor does it. The disagreement between nonempirical and semiempirical geometric parameters in Table I is typical. (The large basis set nonempirical calculations should give geometries in close agreement with experiment.³⁷) To avoid the energy and charge anomalies that restorative forces may produce when electronic structure calculations are carried out at geometries far from those which are optimal for a given model,³⁸ geometric variables were partially optimized. Because the MINDO/3 program^{40,41} available in our laboratory (which uses an extremely efficient geometry optimization algorithm⁴²) could accomplish the desired adjustments automatically, it was used instead of our CNDO programs for this part of the study. Since the system-

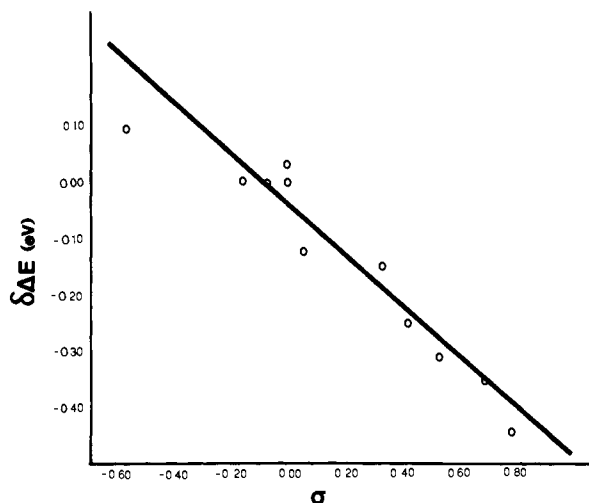


Figure 1. CNDO/2 calculated substituent effects on activation energy (for substituted benzyl chloride-chloride exchange reactions) vs. Hammett σ constants. If the point furthest from the line (4-NH₂) is omitted, the least-squares correlation equation is $\delta\Delta E^\ddagger = (-0.48 \pm 0.04)\sigma + (-0.03 \pm 0.02)$ eV. The correlation coefficient for the ten data is 0.97.

atic geometric distortions characteristic of CNDO/2 are certainly not eliminated by the MINDO/3 approximations^{37,40} and trial optimizations of benzyl chloride and benzyl fluoride using the two approximations produced very similar structures, we feel that the resulting geometries are adequate for our purposes. MINDO/3 geometries were determined for benzene ring and for the -CH₂Cl and -CH₂Cl₂⁻ groups attached to the benzene ring. The geometries of the building blocks were held fixed in subsequent calculations. For comparison with earlier work on simpler S_N2 reactions, geometric parameters for the reaction site are given in Table I.

One indication that our method gives a reasonable account of molecules like those to be considered here is provided by a comparison of available experimental dipole moments for substituted benzenes with the corresponding calculated quantities; such a comparison is made in Table II.

Results and Discussion

On an absolute basis, CNDO/2 does not give a good account of the energetics of S_N2 displacement. Like other workers,^{31,32,34} we found that NDO calculations on our model S_N2 transition states gave energies which were lower than those of the separated reactants (see Table III). (The same phenomenon is observed, though doubtless for different reasons, when basis sets of modest size are used in nonempirical SCF calculations on these systems.^{25,26a,27a}) Trends in energetic effects of *substitution*, however, are very well reproduced. Figure 1 compares calculated energy differences between transition state models and reactants with Hammett σ constants. We feel

Table III. CNDO/2 Energies for Model S_N2 and Related Reactions

X	XC ₆ H ₄ CH ₂ Cl ^a	XC ₆ H ₄ CH ₂ Cl ₂ ^{-a}	XC ₆ H ₅ ^a	$\Delta E(R1)^{b,c}$	$\Delta E(R2)^{b,c}$	$\Delta E^\ddagger{}^c$	$\delta\Delta E^\ddagger{}^c$
H	71.2169	87.4031	47.1035	0.00	0.00	-51.83	0.00
4-NH ₂	83.6815	99.8646	59.5676	-0.34	1.62	-49.88	1.95
3-NH ₂	83.6817	99.8670	59.5676	-0.43	0.12	-51.29	0.55
4-CH ₃	79.9045	96.0907	55.7908	-0.19	-0.19	-51.84	-0.01
3-CH ₃	79.9044	96.0909	55.7908	-0.14	-0.33	-52.03	-0.19
4-F	98.2034	14.3943	74.0904	0.21	-2.72	-54.77	-2.93
3-F	98.2037	114.3953	74.0904	0.08	-3.32	-55.23	-3.39
4-CF ₃	160.8989	177.0964	136.7851	-0.26	-7.35	-58.93	-7.09
3-CF ₃	160.8984	177.0940	136.7851	0.06	-5.82	-57.72	-5.89
4-NO ₂	119.0423	135.2448	94.9288	-0.04	-10.27	-62.06	-10.22
3-NO ₂	119.0413	135.2405	94.9288	0.60	-7.57	-60.00	-8.16

^a Minus E_T , Hartrees. ^b For definitions of reactions R1 and R2, see text. ^c Kcal/mol.

Table IV. Total Electron Densities^{a,b} of Benzyl Chlorides and Model S_N2 Transition States

Molecule	CH ₂	Cl	C ₁	(CH) ₂	(C[H]) ₃	(C[H]) ₄	(CH) ₅	(CH) ₆	Subst.
Benzyl chloride (BC)	-10	15	-4	0	-1	0	-1	0	0 ^c
Model transition state (TS)	-25	11	-10	2	2	5	2	2	3 ^c
Δ(TS - BC)	-15	-4	-6	1	3	5	3	1	3 ^c
4-NH ₂ -BC	-10	16	-1	-2	5	-14	5	-2	2
4-NH ₂ -TS	-25	12	-8	0	7	-11	7	0	7
Δ(TS - BC)	-15	-4	-6	1	2	3	2	1	4
δ(NH ₂ - H)	0	1	3	-2	6		6	-2	
3-NH ₂ -BC	-10	15	-6	6	-14	6	-3	4	3
3-NH ₂ -TS	-25	11	-12	7	-13	10	0	4	6
Δ(TS - BC)	-15	-4	-6	1	-1	5	3	1	4
δ(NH ₂ - H)	0	0	-2	6		6	-2	3	
4-CH ₃ -BC	-10	15	-4	0	1	-4	1	0	0
4-CH ₃ -TS	-25	11	-10	1	3	-1	3	1	5
Δ(TS - BC)	-15	-4	-6	1	2	3	2	1	5
δ(CH ₃ - H)	0	0	1	0	2		2	0	
3-CH ₃ -BC	-10	15	-5	2	-5	2	-1	1	0
3-CH ₃ -TS	-25	11	-11	3	-4	6	2	2	4
Δ(TS - BC)	-15	-4	-6	1	1	5	3	1	4
δ(CH ₃ - H)	0	0	0	2		2	0	1	
4-F-BC	-10	15	-3	-2	2	-22	2	-2	21
4-F-TS	-25	11	-9	-1	4	-19	4	-1	24
Δ(TS - BC)	-15	-4	-6	1	3	3	3	1	3
δ(F - H)	0	0	1	-2	2		2	-2	
3-F-BC	-10	14	-6	3	-22	2	-3	2	21
3-F-TS	-25	11	-12	4	-22	8	0	3	23
Δ(TS - BC)	-15	-4	-6	1	1	5	3	1	2
δ(F - H)	0	-1	-2	3		3	-2	1	
4-CF ₃ -BC	-10	14	-6	0	-5	6	-5	0	6
4-CF ₃ -TS	-25	10	-12	1	-2	9	-2	1	11
Δ(TS - BC)	-15	-4	-6	1	2	3	2	1	4
δ(CF ₃ - H)	0	-1	-2	0	-4		-4	0	
3-CF ₃ -BC	-10	14	-5	-3	5	-4	-2	-2	6
3-CF ₃ -TS	-25	10	-10	-2	6	1	1	-1	10
Δ(TS - BC)	-15	-4	-6	1	1	5	3	1	4
δ(CF ₃ - H)	0	-1	0	-4		-4	-1	-2	
4-NO ₂ -BC	-10	13	-7	0	-6	-3	-6	0	19
4-NO ₂ -TS	-25	9	-13	1	-4	0	-4	1	24
Δ(TS - BC)	-15	-4	-6	1	2	3	2	1	5
δ(NO ₂ - H)	-1	-2	-2	-1	-5		-5	-1	
3-NO ₂ -BC	-10	14	-5	-4	-4	-5	-2	-3	19
3-NO ₂ -TS	-25	10	-11	-3	-3	0	1	-2	23
(TS - BC)	-15	-3	-6	1	1	5	3	1	4
(NO ₂ - H)	-1	-1	0	-5		-5	-1	-3	

^a Relative to formal density at each site. ^b In units of 0.01 electron. ^c Density at H₄.

that this is the most appropriate comparison with experimental data because our desire to study substituent effects (rather than this S_N2 reaction per se) has led us to impose a constancy of reaction site structure which may not be present⁴⁵ in the real systems with which comparisons might otherwise be made.²⁶

A recent (and useful) discussion⁴³ of electronic effects of substituents in benzene derivatives has distinguished no less than seven conceptually separate, physically meaningful modes of transmission of these effects. Since the usual electronic structure calculations produce only an energy and a final electron distribution, their interpretation in these terms is not a trivial task. Libit and Hoffmann⁴⁴ used an extended Hückel perturbation theory to follow the development of substituent effects in hydrocarbons as substituent and skeleton were allowed to interact. This analytical framework allowed separation of effects which appeared as the perturbation was applied to different orders. Hermann⁴⁵ used a separate calculation of the electrostatic field effects of a series of substituents to gauge the importance of this contribution to calculated energy changes. At the present stage of this work, we consider only total energy changes and extract whatever information can be

obtained from a Mulliken population analysis⁴⁶ of the CNDO wave functions; the results of even this simple analysis are quite interesting. More sophisticated approaches, to be applied to these and other systems, are under development.

The observed effects of substitution on activation energy arise primarily from interaction of substituent and reaction site in the (charged) model transition states. Appropriate measures of these interactions, suggested by Reynolds,⁴⁷ are the energy changes for reactions R1 and R2. Calculated values of these

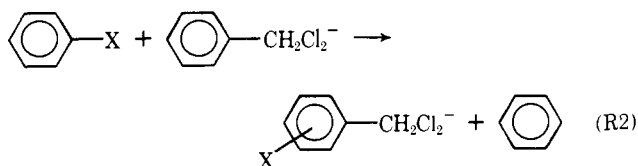
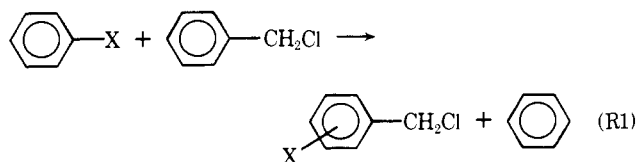


Table V. π Electron Densities^{a,b} of Benzyl Chlorides and Model S_N2 Transition States

Molecule	C _α	C ₁	C ₂	C ₃	C ₄	C ₅	C ₆	Subst. ^c
Benzyl chloride (BC)	-7	-1	1	-1	0	-1	1	
Model transition state (TS)	-18	-8	3	0	5	0	3	
Δ(TS - BC)	-11	-7	2	1	5	1	2	
4-NH ₂ -BC	-8	4	-2	7	-7	7	-2	0
4-NH ₂ -TS	-18	-4	0	6	-1	6	0	0
Δ(TS - BC)	-11	-8	2	0	5	0	2	-1
δ(NH ₂ - H)	-1	5	-3	8	-7	8	-3	
3-NH ₂ -BC	-7	-4	9	-7	8	-4	6	1
3-NH ₂ -TS	-18	-10	10	-6	12	-3	8	0
Δ(TS - BC)	-11	-6	1	1	4	1	1	-1
δ(NH ₂ - H)	0	-3	8	-6	7	-3	5	
4-CH ₃ -BC	-7	0	0	1	-3	1	0	-4
4-CH ₃ -TS	-18	-7	2	1	3	1	2	-5
Δ(TS - BC)	-11	-8	2	0	6	0	2	-2
δ(CH ₃ - H)	0	1	-1	2	-3	2	-1	
3-CH ₃ -BC	-7	-2	4	-4	3	-2	3	-3
3-CH ₃ -TS	-18	-9	5	-2	7	-1	4	-5
Δ(TS - BC)	-11	-7	1	1	4	1	1	-1
δ(CH ₃ - H)	0	-1	2	-3	2	-1	1	
4-F-BC	-7	1	0	3	-2	3	0	-4
4-F-TS	-18	-6	2	3	3	3	2	-4
Δ(TS - BC)	-11	-7	2	0	5	0	2	0
δ(F - H)	0	2	-2	4	-2	4	-2	
3-F-BC	-6	-3	6	-3	4	-3	4	-4
3-F-TS	-17	-10	8	-3	9	-2	5	-4
Δ(TS - BC)	-11	-7	2	1	5	1	2	0
δ(F - H)	1	-2	4	-2	4	-2	2	
4-CF ₃ -BC	-6	-4	2	-3	6	-3	2	-26
4-CF ₃ -TS	-17	-11	4	-3	12	-3	4	-27
Δ(TS - BC)	-11	-7	2	0	6	0	2	-1
δ(CF ₃ - H)	1	-3	0	-2	6	-2	0	
3-CF ₃ -BC	-6	-1	0	4	-1	-1	-1	-26
3-CF ₃ -TS	-17	-8	1	5	3	0	1	-27
Δ(TS - BC)	-11	-7	2	1	5	1	2	-1
δ(CF ₃ - H)	1	0	-2	5	-2	0	-2	
4-NO ₂ -BC	-6	-5	2	-4	7	-4	2	-5
4-NO ₂ -TS	-17	-13	4	-4	13	-4	4	-7
Δ(TS - BC)	-11	-7	2	0	6	0	2	-2
δ(NO ₂ - H)	1	-4	1	-3	7	-3	1	
3-NO ₂ -BC	-6	-1	-1	6	-3	-1	-2	-5
3-NO ₂ -TS	-17	-8	0	7	2	0	-1	-7
Δ(TS - BC)	-11	-7	2	1	4	1	2	-2
δ(NO ₂ - H)	1	0	-3	7	-3	0	-3	

^a Relative to formal density at each atom. ^b In units of 0.01 electron. ^c Atom adjacent to ring only.

energy changes, and their differences the substituent effects on activation energy, are given in Table III.

Calculated total atomic charges for substituted benzyl chlorides and model transition states are given in Table IV. To avoid the possibility of attaching undue importance to an uncertain balancing of charge distributions which is a sensitive function of semiempirical parameter choice,^{17a,48} the electron densities of a carbon atom and its attached hydrogen atoms are combined into a "regional"^{17a} electron density which is associated with the carbon. All densities are measured relative to the formal density of the atom or group, in units of 0.01 electron. (This was the highest level of sensitivity which did not respond to quite modest geometric distortions.)

The most striking feature of these data is that, to within one or two hundredths of an electron, *there are no differences between the charge perturbations produced by the substituents in benzyl chlorides and in model transition states*. Equivalently, it is the *difference in energetic response of a relatively constant benzyl chloride-transition state charge development pattern to relatively constant substituent charge perturbation patterns* which give rise to the calculated substituent effects on activation energy. Changes in either substituent charge

perturbations or reaction site charge development pattern as benzyl chloride is transformed into model transition state are of much more limited importance. Thus, at least in this system, the common supposition that substituent effects arise from differences in induced electron density changes at the reaction site (and that σ constants reflect such charge perturbations) is most inadequate.

The parent compounds can be examined as prototypes for the charge development pattern of the reaction: the mutual perturbation of benzene nucleus and reaction site in benzyl chloride and unsubstituted model transition state are representative of these effects in all systems examined. Before reaction, the $-\text{CH}_2\text{Cl}$ group accepts 0.05 electron from the ring, almost entirely from the σ system; the π system (see Table V) is essentially unperturbed. In the model transition state, the (now negatively charged) $-\text{CH}_2\text{Cl}_2^-$ group donates 0.03 electron to the ring. The net donation of 0.08 electron which occurs as the reaction proceeds is almost completely a π electron effect, part of it uniform (0.01 electron at each ring carbon), part of it concentrated at the positions ortho (0.02 electron each) and para (0.04 electron) to the carbon at which the reaction site is attached.⁴⁹

In view of the vanishingly small response of substituent charge perturbations to transformation of the reaction site from $-\text{CH}_2\text{Cl}$ to $-\text{CH}_2\text{Cl}_2^-$, it is not surprising that these perturbations are also rather insensitive to the relative orientation (meta or para) of substituent and reaction site. (This is assumed in many qualitative discussions of substituent effects in benzene derivatives.) Putting aside the question of mechanism (e.g., mesomeric vs. π inductive, etc.), the substituents behave about as one would expect. The amino group produces minimal net transfer of charge between ring, reaction site, and substituent but is both a strong donor to and a strong polarizer of the π electron system of the ring. As Libit and Hoffmann⁴⁴ found in their examination of the parent benzene system, the methyl group here acts almost exclusively as a π polarizer. Fluorine, as befits an atom with its high electronegativity, is a strong net acceptor of electron density, most of it coming from the σ system of the benzene ring; it also acts as a moderate π donor and polarizer. In accord with an electrostatic (but not with an inductive) model of its action,⁵⁰ the trifluoromethyl group is only a very moderate net acceptor in these molecules; its main effect on the π system of the ring is a polarization of electron density. Finally, the nitro group is a strong electron acceptor, drawing significant amounts of charge from both ring (mainly its σ system) and reaction site (mainly its π system).

In none of these molecules is the operation of a long-range classical inductive effect⁵¹ evident. Like other groups,⁵² we observe an alternation of charge perturbation in both π and σ systems which falls off quite rapidly. These calculations thus lend some support to those who have argued that what is often considered an inductive effect is in most cases not that, but rather an electrostatic field effect.⁵³ The calculated σ charge perturbations could not be simply correlated with "inductive"¹⁰ or "field"⁹ substituent constants, indicating that these latter quantities reflect a transmission process which is not dominated by perturbation of σ charges in the ring.

The energy perturbations (of the order of a few kilocalories per mole) which substituents produce in the reactions of benzene derivatives are generally smaller in magnitude than the absolute errors in the best current quantum mechanical calculations on polyatomic molecules. This alone argues for caution in using any electronic structure calculation to explore these effects. Nevertheless, even crude calculations like those reported here seem to mirror the experimental substituent effects fairly well. The detailed picture of structural and electronic change such calculations provide may, if interpreted with due respect for the vast body of empirical data which have been collected for these systems, be an important key to the predictive understanding which is the common goal of theory and experiment.

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Studies of Hydrogen Bonding in the Vapor Phase by Measurement of Thermal Conductivity and Molecular Orbital Calculations. 2,2,2-Trifluoroethanol[†]

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Abstract: The thermal conductivity of 2,2,2-trifluoroethanol vapor was measured in a modified thick hot-wire cell between 338 and 385 K at pressures ranging from approximately 100 to 1300 Torr (13.3–173 kPa). Analysis of the data indicates that molecular association to form a dimeric species is the main source of the enhancement of the thermal conductivity of the vapor. The enthalpy of association of the trifluoroethanol dimer is -4753 cal/mol and the entropy of association is -18.73 cal/mol K. Ab initio calculations were carried out on several rotational isomers of trifluoroethanol and on four possible dimer structures. The most stable dimer is a cyclic structure involving the gauche-staggered isomer of trifluoroethanol. An extra hydrogen bond due to the presence of the fluorines enhances the stability of the dimer compared to the methanol dimer.

I. Introduction

In this paper, we report a study of the hydrogen bonding in 2,2,2-trifluoroethanol vapor by the measurement of thermal conductivity as a function of pressure^{1,2} and by use of molecular orbital calculations.

Information concerning the association of 2,2,2-trifluoroethanol (TFE) in the vapor is of interest for two reasons. First, experimental and theoretical determination of the strength of the attraction between TFE molecules can provide fundamental insights into the effect of the CF_3 substituent on the association properties of alcohols. Second, the thermal conductivity measurements can provide some important thermodynamic data on TFE which is lacking in the literature despite its potential use as a working fluid in power cycles.³

A number of studies of association in alcohols have been made using PVT, heat capacity, and thermal conductivity measurements.⁴ Although there are often large discrepancies between conclusions reached from different studies on alcohols, the majority of workers have deduced the presence of dimers and many have deduced the presence of higher polymers. The thermal conductivity technique developed in this laboratory^{1,2} has proved successful in a study of association in methanol vapor.¹ This technique uses the pressure dependence of the thermal conductivity of a gas to determine which associated species are present and their thermodynamic properties.

In thermal conductivity measurements on TFE vapor reported here, the presence of a dimeric species has been determined. The equilibrium constant and enthalpy and entropy of association for the dimer are evaluated from the data. No higher polymers are detected as in the case of methanol vapor.

There have been few ab initio molecular orbital studies of association between alcohol molecules. The only studies have been done on small clusters of methanol molecules.^{5,6} The

application of a single technique such as the thermal conductivity method to a number of alcohol vapors, TFE being the second, should provide consistent data for comparison with ab initio calculations. Hence, as a part of this study, we have carried out minimal basis set SCF calculations on hydrogen bonding between TFE molecules. Calculations were first performed on the various rotational isomers of the TFE monomer and then the lowest energy isomers were used in forming different dimer structures. The most stable dimer is found to have a cyclic hydrogen bond and has a stronger hydrogen bond than the methanol dimer. The hydrogen bond strengths are consistent with the experimental results. The structures of the monomer and dimer are used to help explain why no higher polymers are observed in TFE vapor as in the case of methanol vapor.

II. Experimental Section

A. Apparatus. The thermal conductivity of 2,2,2-trifluoroethanol was measured at five temperatures between 338 and 385 K and at pressures ranging from 100 to 1300 Torr. The apparatus employed was a modification of the thick hot-wire cell described by Kannuliuk and Carman.⁷ A platinum wire, 0.508 mm in diameter, was mounted along the axis of a precision-bore soft glass tube which was 101.6 mm long and had an internal diameter of 4.999 ± 0.005 mm. This tube was fabricated from soda lime glass whose coefficient of thermal expansion was matched to that of the platinum wire. The wire was secured at each end of the tube by directly fusing it to the soft glass while applying slight tension to maintain proper alignment. The cell was made vacuum tight by coating the glass-to-metal seals with a thin layer of low vapor pressure Torr Seal epoxy. Samples were admitted to the conductivity cell through a small hole in the tube wall near one end.

The cell assembly was submerged in a 15-gal bath filled with Dow Corning 710 silicone fluid. The temperature of the oil was maintained to within about ± 0.005 °C by a Bailey Model 124 precision temperature controller. The bath temperature was measured with a platinum resistance thermometer accurate to ± 0.001 °C.

A series of valves permitted stepwise reduction of pressure within the system. Pressures were measured with a Statham Model PA822

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