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Intermolecular Self-Consistent-Field Perturbation Theory for Organic Reactions. 1. Theory and Implementation; Nucleophilic Attack on Carbonyl Compounds

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Abstract: We report an implementation of Basilevsky and Berenfeld's intermolecular SCF perturbation theory as an extension to the GAUSSIAN-70 SCF package. The intermolecular interaction energy is computed as a sum of electrostatic, exchange, exchange-repulsion, charge-transfer, and polarization energies, each of which can be analyzed further if required. The results are in excellent agreement with supermolecule SCF calculations. Results are presented for calculations on some reactions involving nucleophilic attack on carbonyl groups, and the reasons for the directional nature of the attack are studied. It emerges that the closed-shell repulsion, the electrostatic interaction, and the charge-transfer term must all be taken into account, and that a frontier-orbital description of the charge-transfer term is inadequate in general, though Baldwin's approach-vector model can be usefully understood in frontier-orbital terms.

I. Introduction

Much of organic chemistry is concerned with reactions between closed-shell molecules in their ground states, which can often be adequately described in terms of single-configuration SCF wave functions. Where the reaction is thermally allowed in the Woodward–Hoffmann sense,[1,2] the system continues to be adequately described by a single-configuration wave function throughout the reaction path. An intermolecular perturbation theory which takes the molecular SCF wave functions as the starting point may then allow a useful comparison between competing reaction pathways, by providing comparative interaction energies at points along the respective reaction coordinates.

The present work has been motivated by the need for a nonempirical theory for organic chemistry which includes all the Hartree–Fock terms in the interaction energy and which yields its result in a form which can be readily compared with the Klopman–Salem equation.[3-5] This equation is widely used by organic chemists, but its original derivation was not very rigorous, and drastic approximations are frequently made in its application.

It expresses the interaction energy as the sum of three terms: the closed-shell repulsion, the Coulombic or electrostatic interaction, and the attractive charge-transfer term. The last of these arises from the mixing of vacant orbitals on one molecule into occupied orbitals on the other and is frequently approximated by the "frontier orbital" term involving the lowest unoccupied molecular orbital (LUMO) of the more electrophilic species and the highest occupied one (HOMO) of the other. Also the closed-shell repulsion energy is often assumed to be the same for several competing reaction paths and is therefore ignored. Then reactions are described as "charge controlled" or "orbital controlled" according to whether the electrostatic or frontier-orbital term, respectively, is dominant. The theory is very successful in many applications,[5] but exceptions are not uncommon, and the theory has been criticized in both practical[6] and theoretical[2] terms.

In this paper we describe the implementation of Basilevsky and Berenfeld's intermolecular perturbation theory for regions of small overlap,[7] subsequently referred to as BB. Their formalism is different from others which have been used for this purpose[8] in its treatment of the permutational symmetry problem and the nonorthogonality problem.[9] The unperturbed wave function is taken to be the solution of the Hartree–Fock problem when all intermolecular matrix elements (including overlap integrals) are set to zero and is a single Slater determinant containing the occupied orbitals of both noninteracting molecules. Consequently it has the full electron-permutation symmetry of the interacting system. The perturbation is then developed as a double series in the intermolecular part of the Fock matrix and in the intermolecular overlap.[10] This approach includes two-electron as well as one-electron perturbations in the Fock matrix, so extending earlier formulations of SCF perturbation theory.[11] It complements the method used by Morokuma,[12] who obtains the various terms in the interaction by performing SCF calculations on the complete interacting system ("supermolecule" calculations) in which certain parts of the interaction have been set to zero. In this way he is able to obtain the separate terms in the Klopman–Salem equation without relying on the approximations of perturbation theory, but his method does not, as ours does, allow the terms to be further analyzed in order to identify, for example, the molecular orbitals (if any) which dominate the charge-transfer interaction, or the important atomic repulsions or attractions in the exchange repulsion or the electrostatic energy. We have, on the other hand, been able to check that the perturbation calculation gives results that agree well with those obtained from a supermolecule calculation, so we believe that the analysis of the perturbation theory results is valid. Attempts to use perturbation theory where the interaction is very strong are bound to fail, but we have found the range of validity of the method to be adequate for our purposes, especially as we have been able to extend the range by incorporating a simple modification to correct for incipient divergence of the perturbation formula.

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II. Derivation of Formulas in the AO Basis

We give first a resumé of the notation. Subscripts a, b, etc. are used to label molecular orbitals on molecule A, and a′, b′, etc. are used similarly for molecule A′. If it is necessary to distinguish occupied and virtual molecular orbitals, we use the letter n for the former and v for the latter, again with primes for molecule A′. This is different from BB's notation, which uses additional subscripts 1 and 2 to denote occupied and virtual orbitals. We use the transformation II.1 between molecular orbitals φ_a and the

$$\varphi_{a} = \sum_{r} \chi_r C_{ra}$$

$$\varphi_{a'} = \sum_{r'} \chi_{r'} C_{r'a'} \tag{II.1}$$

atomic orbital basis χ_r; we shall use the subscripts p, q, r, s, . . . to label atomic orbitals on molecule A, and again primes refer to molecule A′.

The zeroth-order density matrix in the AO basis is defined by

$$P_{rs} = 2(\mathbf{C}\mathbf{R}^{(0)}\mathbf{C}^{\dagger})_{rs} = 2\sum_{n} C_{rn} C_{sn}$$

$$P_{r's} = 0 \tag{II.2}$$

where $\mathbf{R}^{(0)}$ is the zeroth-order density matrix in the MO basis. Here, and subsequently, similar equations apply with primes/no primes exchanged. We follow BB in using the overlap matrix T defined in terms of the molecular orbitals:

$$\mathrm{T} = \mathbf{1} + \mathbf{t} \tag{II.3}$$

where **t** is the off-diagonal (i.e., intermolecular) part of the overlap matrix and is related to the corresponding matrix $\bar{\mathbf{t}}$ in the AO basis by

$$\mathbf{t} = \mathbf{C}^{\dagger}\bar{\mathbf{t}}\mathbf{C} \tag{II.4}$$

Here, and subsequently, we use a bar to denote a matrix in the AO basis, unless a specific element appears, when the nature of the subscripts serves to distinguish between the two bases. Similarly no special notation is required to distinguish between two-electron integrals in the two bases, since the orbital labels show which is intended.

Expressions were obtained by BB for the electrostatic (or Coulomb) energy E_{elec}, the exchange energy E_{ex}, the exchange repulsion energy E_{er}, the charge-transfer (or resonance) energy E_{ct}, and the polarization energy E_{pol} which together comprise the SCF interaction energy to second order. Some of the formulas (eq 7, 8, and 11 of ref 7) have typographical errors, however, and a factor of 2 is missing in the expressions for E_{ct} and E_{pol}, so the formulas are repeated here in their correct form.[13] We consider these formulas in turn and show briefly how they have been expressed in the AO basis for computational purposes. Basilevsky and Berenfeld carried out a similar analysis[7] but used the CNDO approximations.

Electrostatic (Coulomb) Energy. In this expression, $W_N^{AA'}$

$$E_{elec} = 2\sum_{n} U_{nn}^{A'} + 2\sum_{n'} U_{n'n'}^{A} + 4\sum_{nn'} (nn|n'n') + W_N^{AA'} \tag{II.5}$$

is the nuclear–nuclear repulsion energy, U^A and $U^{A'}$ are the potentials due to the nuclei on molecules A and A′, respectively, and (nn|n′n′) is an electron repulsion integral. Use of the transformation of eq II.1 together with eq II.2 yields an expression in a convenient form for computation:

$$E_{elec} = \sum_{rs} P_{rs} U_{rs}^{A'} + \sum_{r's'} P_{r's'} U_{r's'}^{A} + \sum_{rsr's'} P_{rs} P_{r's'} (rs|r's') + W_N^{AA'} \tag{II.6}$$

This term corresponds to the electrostatic energy of long-range perturbation theory and also to the electrostatic term of the Klopman–Salem equation.

Exchange Energy.

$$E_{ex} = -2\sum_{nn'} (nn'|n'n) \tag{II.7}$$

This also is readily transformed to the AO-based form

$$E_{ex} = -\frac{1}{2} \sum_{rsr's'} P_{rs} P_{r's'} (rr'|ss') \tag{II.8}$$

This term has no analogue in the Klopman–Salem equation, and because it depends on overlap it is absent from the long-range theory. It is strongly attractive at short range.

Exchange Repulsion Energy. In this expression, **L** is the Fock

$$E_{er} = -\mathrm{Tr}\mathbf{R}^{(0)}[\mathbf{t},\mathbf{M}]_{+} + \tfrac{1}{4}\mathrm{Tr}\mathbf{R}^{(0)}[\mathbf{t},[\mathbf{t},\mathbf{L}]] \tag{II.9}$$

matrix for the composite system AA′, except that it involves the zeroth-order density matrix $\mathbf{R}^{(0)}$ (i.e., **P**) rather than the full density matrix **R** and neglects the nonorthogonality between molecular orbitals on different molecules. However the matrix **M**, given by

$$\mathbf{M} = \mathbf{L} - \tfrac{1}{2}[\mathbf{t},\mathbf{L}]_{+} \tag{II.10}$$

incorporates a correction for this nonorthogonality to first order in the intermolecular overlap **t**. In the AO basis **L** is

$$L_{pq} = K_{pq} + U_{pq}^{A} + U_{pq}^{A'} + \sum_{rs} P_{rs}[(pq|rs) - \tfrac{1}{2}(pr|qs)] \tag{II.11}$$

where **K** is the kinetic energy operator, while **M** becomes

$$\bar{\mathbf{M}} = \bar{\mathbf{L}} - \tfrac{1}{2}(\bar{\mathbf{t}}\bar{\mathbf{B}}\bar{\mathbf{L}} + \bar{\mathbf{L}}\bar{\mathbf{B}}\bar{\mathbf{t}}) \tag{II.12}$$

where

$$\bar{\mathbf{B}} = \mathbf{C}\mathbf{C}^{\dagger} \tag{II.13}$$

The exchange repulsion energy then becomes

$$E_{er} = -\tfrac{1}{2}\mathrm{Tr}\bar{\mathbf{M}}\bar{\mathbf{X}} + \tfrac{1}{2}\mathrm{Tr}\bar{\mathbf{L}}\bar{\mathbf{Z}} \tag{II.14}$$

where

$$\bar{\mathbf{X}} = \bar{\mathbf{B}}\bar{\mathbf{t}}\bar{\mathbf{P}} + \bar{\mathbf{P}}\bar{\mathbf{t}}\bar{\mathbf{B}} \tag{II.15}$$

and

$$\bar{\mathbf{Z}} = \tfrac{1}{4}[\bar{\mathbf{P}}\bar{\mathbf{t}}\bar{\mathbf{B}}\bar{\mathbf{t}}\bar{\mathbf{B}} + \bar{\mathbf{B}}\bar{\mathbf{t}}\bar{\mathbf{B}}\bar{\mathbf{t}}\bar{\mathbf{P}} - 2\bar{\mathbf{B}}\bar{\mathbf{t}}\bar{\mathbf{P}}\bar{\mathbf{t}}\bar{\mathbf{B}}] \tag{II.16}$$

The first term in eq II.14 is repulsive (i.e., $\mathrm{Tr}\bar{\mathbf{M}}\bar{\mathbf{X}} < 0$) and is the dominant term; it corresponds to the repulsive term of the Klopman–Salem equation. The second term is attractive. In analyzing the effect of E_{er} it is sometimes useful to consider

$$Q_{rs'} = M_{rs'} X_{s'r} \tag{II.17}$$

as representing the exchange repulsion between AOs r and s′. A sum of these contributions over all AOs r on one atom and s′ on another then gives the exchange repulsion between a pair of atoms. A similar treatment can be applied to the electrostatic term E_{elec}, yielding atom–atom, atom–bond, and bond–bond contributions.

Charge-Transfer (Resonance) Energy.

$$E_{ct} = 2\sum_{nv'} |M_{nv'}|^2/(\epsilon_n - \epsilon_{v'}) + 2\sum_{n'v} |M_{n'v}|^2/(\epsilon_{n'} - \epsilon_v) \tag{II.18}$$

The matrix **M** is given by eq II.10, and ϵ_n etc. are the orbital energies (Fock matrix eigenvalues) for the noninteracting molecules. This term corresponds directly to the charge-transfer term of the Klopman–Salem equation.

Polarization (Induction) Energy.

$$E_{pol} = 2\sum_{nv} |V_{nv}^{A'}|^2/[\epsilon_n - \epsilon_v - (nv|nv)] + 2\sum_{n'v'} |V_{n'v'}^{A}|^2/[\epsilon_{n'} - \epsilon_{v'} - (n'v'|n'v')] \tag{II.19}$$

The matrix $\mathbf{V}^A$ is given in the AO basis by

$$V_{rs}^{A} = 0$$

$$V_{rs'}^{A} = 0$$

$$V_{r's'}^{A} = U_{r's'}^{A} + \sum_{rs} P_{rs}(r's'|rs) \tag{II.20}$$

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[13] R. W. Erskine, Ph.D. Thesis, University of Cambridge, 1979.

We write the interaction energy obtained from the sum of these energy terms as

$$\Delta E_{\text{pert}} = E_{\text{elec}} + E_{\text{er}} + E_{\text{ex}} + E_{\text{ct}} + E_{\text{pol}} \tag{II.21}$$

and distinguish it from the interaction energy calculated as the difference between the SCF variational energies for the combined and separated systems:

$$\Delta E_{\text{scf}} = E_{\text{AA}'} - E_{\text{A}} - E_{\text{A}'} \tag{II.22}$$

We have routinely calculated ΔE_{scf} in order to check that the perturbation theory gives results in reasonable agreement with the full supermolecule SCF calculation. Only when this is true, as it usually is, can the analysis of the perturbation calculation be expected to yield useful results.

A third expression can be obtained if we take account of basis set extension effects[14] by including "ghost orbitals" in the evaluation of the energies of the separated molecules to obtain values E_{A}^{g} and $E_{\text{A}'}^{\text{g}}$:[15]

$$\Delta E_{\text{g}} = E_{\text{AA}'} - E_{\text{A}}^{\text{g}} - E_{\text{A}'}^{\text{g}} \tag{II.23}$$

ΔE_{g} is higher than ΔE_{scf} (more positive) and is a better measure of the activation energy. We refer to ΔE_{scf} or ΔE_{g} as "variational" interaction energies for brevity, though of course these energy differences are not themselves bounded variationally.

Computational Details. In our calculations we used the GAUSSIAN-70 package,[16] with extensive modifications, as follows:

(i) The geometry input routine was modified to allow a system to be specified as two (or more) molecules or fragments, whose positions and orientations can be altered independently without any change to the specification of the internal coordinates of each fragment. In the rest of the program, nuclei and basis functions can be identified as belonging to a particular fragment.

(ii) The one-electron integral routines have been modified to allow any of the following options: (a) all integrals calculated (supermolecule calculation); (b) intermolecular integrals omitted (allowing simultaneous calculation of E_{A} and $E_{\text{A}'}$); (c) all integrals calculated, but nuclear potential included for only one molecule (allowing a ghost orbital calculation for that molecule); and (d) intermolecular integrals calculated separately (for the perturbation calculation).

(iii) The two-electron integral routines have been similarly modified to allow intermolecular integrals to be omitted or included or calculated separately. Note that if the relative orientation of two fragments is changed without any change of internal coordinates, then only the intermolecular integrals need be recalculated.

These modifications make it a straightforward matter to compute the various energy terms, variational and perturbational, that have been listed above. We have used a minimal (STO-3G) basis for the calculations reported below, but any basis can be used. The time required for the calculations is quite modest; the calculation of all the perturbational energy terms requires approximately the same computational time as the supermolecule SCF calculation. In particular it is not necessary, as claimed by Kitaura and Morokuma,[12] to carry out a four-index transformation before the charge-transfer terms can be calculated, while for the polarization energy, only a few of the electron-repulsion integrals are needed in the MO basis, so that a full four-index transformation is not needed here either.

III. Convergence of the Perturbation Expansion

Two distinct questions of convergence arise, namely the convergence of the perturbation expansion itself, as usually understood, and the convergence of the overlap expansion. The latter can be investigated with the help of Gerschgorin's theorem,[17] which provides an upper bound to the spectral radius ρ of the intermolecular overlap matrix:

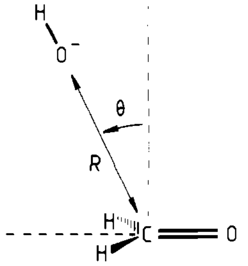

Figure 1. Symmetrical attack of hydroxide ion on formaldehyde. The atoms H–O···C′ are assumed to be collinear.

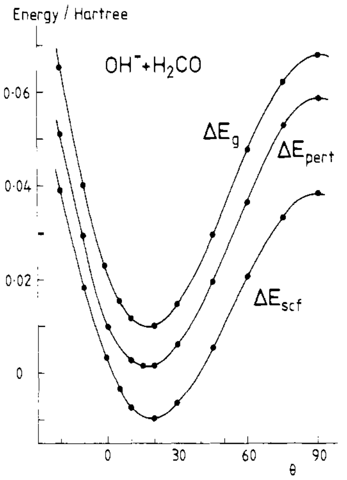

Figure 2. Perturbational energy ΔE_{pert} and variational energies ΔE_{scf} (without ghost orbitals) and ΔE_{g} (with ghost orbitals) for various directions of attack of hydroxide ion on formaldehyde. O···C′ distance = 2 Å.

$$\rho \equiv \max|\lambda_i| \leq \tilde{\rho} = \max_i \sum_{j \neq i} t_{ij} \tag{III.1}$$

where the λ_i are its eigenvalues. The overlap expansion will converge only if $\rho < 1$ and will not converge well unless it is much smaller than 1. We found that good agreement with the variational calculations was obtained for $\tilde{\rho} \leq 0.6$ but that agreement was unsatisfactory when $\tilde{\rho} > 1$. It seems[17] that Gerschgorin's theorem gives a rather loose upper bound for three-dimensional cases, $\tilde{\rho}$ being about 50% larger than ρ.

The convergence of the perturbation expansion as such depends on the energy denominators being large compared with the perturbation matrix elements. This requirement may not always be satisfied for the frontier-orbital contributions to the charge-transfer energy (eq II.18), where the energy difference between the HOMO of an electron donor and the LUMO of an acceptor can be quite small.

We have incorporated into the program a procedure for correcting the result by carrying out approximate degenerate perturbation theory in such cases. This can be done without too much difficulty in the common case where the trouble arises from the near degeneracy of one occupied orbital n in one molecule and one virtual orbital v′ in the other, so that just one term in one of the sums in eq II.18 becomes excessively large. In such a case it can be shown[13] that the offending term should be replaced by

$$\Delta_{\text{nv}'} = \tfrac{1}{2}\{(\epsilon_{\text{v}'} - \epsilon_{\text{n}}) - [(\epsilon_{\text{v}'} - \epsilon_{\text{n}})^2 + 8|M_{\text{nv}'}|^2]^{1/2}\} \tag{III.2}$$

All our calculations of the charge-transfer energy incorporate this correction where necessary. Only rarely was the correction more

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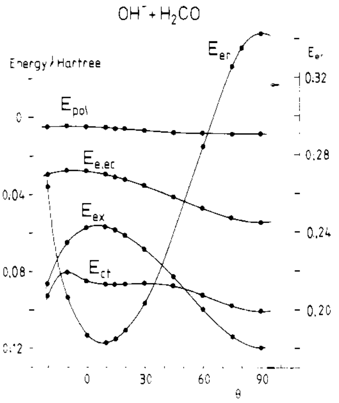

Figure 3. Contributions to the perturbational energy ΔE_{pert} for various directions of attack of hydroxide ion on formaldehyde. O···C′ distance = 2 Å.

than 10% of the total charge-transfer energy, and in such cases the charge-transfer contribution was not a dominant part of the interaction energy.

IV. Nucleophilic Attack of Hydroxide Ion on the Carbonyl Group

Our first applications of chemical interest were concerned with nucleophilic attack on the carbonyl group. Interest in this reaction stems from the experimental work of Bürgi, Dunitz, and Shefter.[18] We have studied the reactions between NH_3 and formaldehyde and between OH^- and formaldehyde as models for this type of reaction.

The geometry used for the hydroxide calculation is illustrated in Figure 1. Results are given in Figures 2 and 3 for various values of the angle θ at a constant O···C distance of 2 Å. In these calculations we took account of the diffuseness of the orbitals in the negative ion by reducing the orbital exponent for the hydroxide oxygen 2s and 2p shell from 2.25 to an optimized value of 2.10. Figure 2 shows that the perturbation calculation is in excellent agreement with the variational ones. The difference between the perturbational and variational energies is not only small, but almost independent of θ, and since we are interested only in relative energies for different reaction paths it can be ignored. This difference is made up of higher-order terms in the perturbation expansion, including cross-terms between the various effects described above, and so can be compared with the "MIX" term of Morokuma's analysis.[12] In this case the curves have minima at $\theta \approx 16.6°$ (for ΔE_{pert}) and $\theta \approx 17.7°$ (for ΔE_g), which both lie within the experimental range of 17 ± 5° for the attack of amines at a carbonyl group.[18] They also agree with the calculation of Bürgi, Lehn, and Wipff,[19] who carried out SCF calculations on the $H^- + H_2CO$ system, optimizing the geometry at each relative configuration of the reactants. Although we have not attempted any geometry optimization, our results are similar in their prediction of the reaction path; the optimization has very little effect at this distance, the carbon atom having moved only 0.15 Å out of the formaldehyde plane at an $H^-\cdots C$ distance of 2 Å. We may therefore analyze the perturbation results with confidence.

The details are shown in Figure 3, and we see that the most important contribution to the perturbation energy is the exchange repulsion E_{er}, which is largely responsible for the shape of the ΔE_{pert} curve. The exchange energy mirrors the exchange-repulsion energy across the whole range of θ; indeed we have found that E_{ex} is quite generally about minus one-third to minus one-quarter of E_{er}. At present we have no explanation of this fact, but it does mean that these two terms can conveniently be considered together under the heading of steric effects. The other terms in the perturbation energy vary much less with θ. The charge-transfer energy is the largest in magnitude, but none is negligible except the polarization energy, and that would be larger if a more flexible basis were used. The electrostatic and charge-transfer terms both favor the direction θ = 90° corresponding to attack along the bisector of the HCH angle, but are heavily outweighed by the exchange-repulsion term. Note that the energy difference between ΔE_{pert} and ΔE_{scf} or ΔE_g, at about 0.015 hartree, is small compared with the perturbational contributions, so we are not neglecting important effects by omitting higher-order terms in the perturbation expansion.

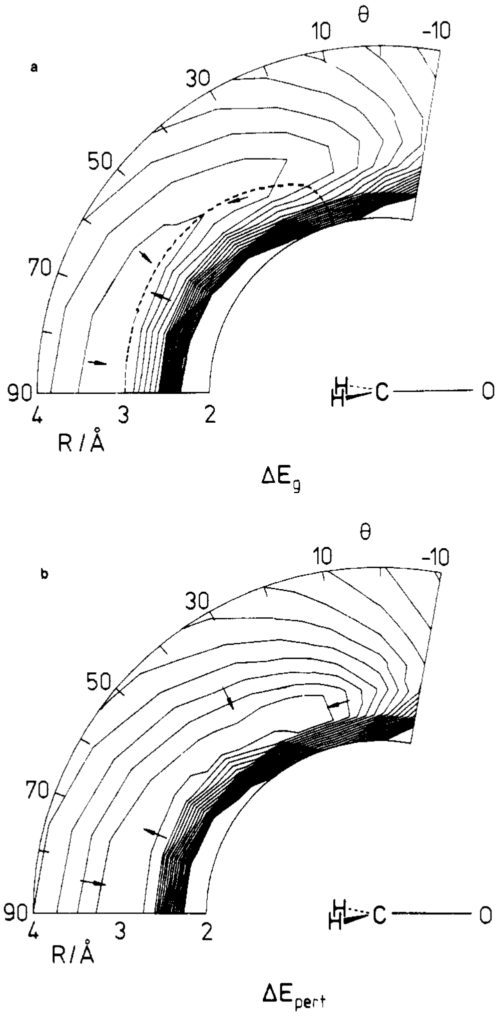

Figure 4. Reaction of OH^- with H_2CO. Contours of (a) SCF interaction energy, calculated with ghost-orbital correction for basis-set superposition error, and (b) total perturbational energy, as a function of the position of the hydroxide oxygen in relation to the formaldehyde molecule. Contour interval 1.2×10^{-3} hartree. The arrows point toward low energy. Contours above 0.013 hartree have been omitted for clarity.

Further calculations were done at 70 points in the region 2 Å ≤ R ≤ 4 Å and −10° ≤ θ ≤ 90°, and the results are presented by contour plots, which give in Figure 4 the SCF interaction energy and the total perturbational energy and in Figure 5 the electrostatic, exchange, exchange-repulsion, and charge-transfer contributions to the perturbational energy. The irregular appearance of many of the contours is an artifact of the plotting program used.

It can be seen that the plots for ΔE_g and ΔE_{pert} are in agreement as to the general features of the potential energy surface. They both predict a minimum in the interaction energy at θ = 90°, $R \approx 3$ Å, and from there the reaction path, shown by the dashed line in Figure 4a, proceeds to $\theta \approx 40°$ at almost constant R, before turning toward the carbon atom to reach R = 2 Å at $\theta \approx 17°$. This behavior is very similar to that reported by Bürgi, Lehn, and Wipff,[19] though as they optimized the H_2CO geometry at each intermolecular configuration, they were able to follow the reaction

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[18] H. B. Bürgi, J. D. Dunitz, and E. Shefter, *J. Am. Chem. Soc.*, **95**, 5065–5067 (1973); *Acta Crystallogr., Sect. B*, **B30**, 1517–1527 (1974).

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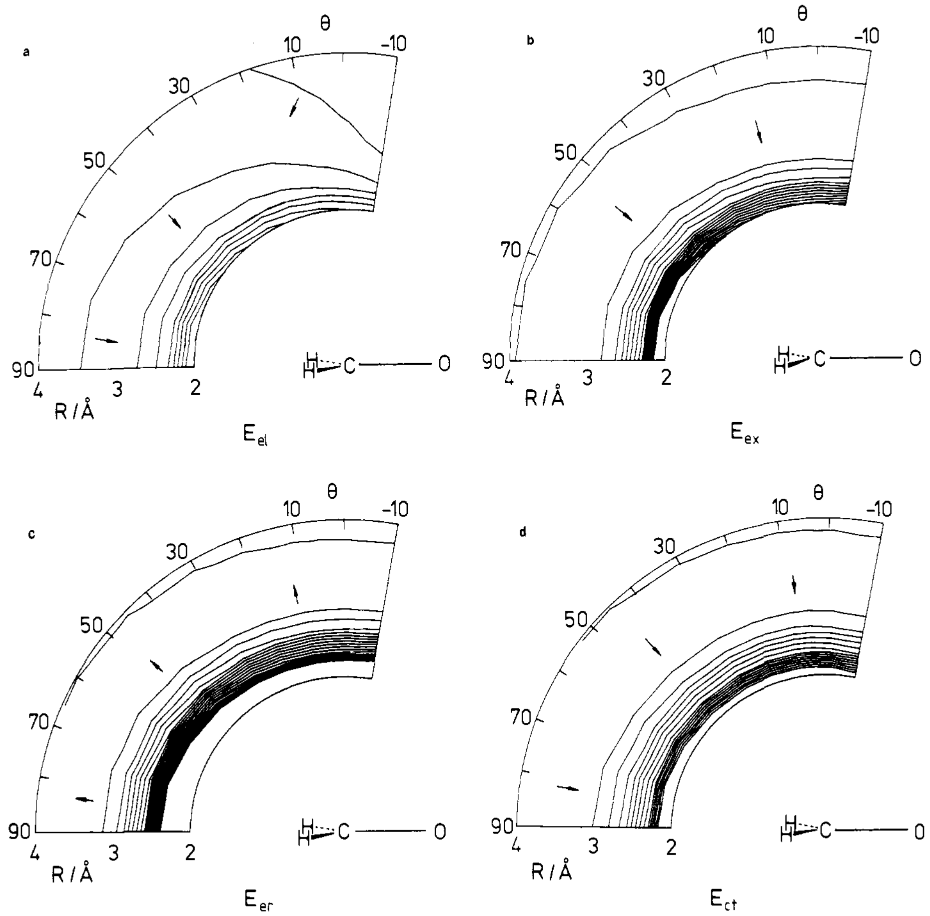

Figure 5. Contours of (a) electrostatic, (b) exchange, (c) exchange-repulsion, and (d) charge-transfer contributions to the perturbational energy for the reaction of OH^- with H_2CO. Contour interval 5×10^{-3} hartree. The arrows point toward low energy. Some contours near $R = 2.0$ Å have been omitted for clarity.

coordinate through to the product. Our interest however lies more in the early stages of the reaction, where we seek to study the influence on the reaction path of the various contributions to the energy, and where, as mentioned above, the geometry of the formaldehyde molecule is little changed.

We see from the contour plots in Figure 5 how the exchange, exchange-repulsion, and charge-transfer terms, depending as they do on overlap, decay exponentially with increasing R, although the contouring routine does not display the exponential behavior particularly well, because the grid points are rather widely separated and linear interpolation is used between them. The electrostatic energy decays much more slowly (in the limit of large R it would behave like R^{-2}) and it is therefore the dominant term in the interaction at values of R near 4 Å and is largely responsible for the well at $R = 3$ Å, $\theta = 90°$. The electrostatic energy can be analyzed into atom–atom, atom–bond and bond–bond contributions, and it then emerges that the atom–bond interactions between the hydroxide oxygen atom and the formaldehyde bonds largely cancel, the oxygen–oxygen contribution varies only slightly at this separation over the range of θ studied, and the main contribution to the electrostatic term is the attraction between the hydroxide oxygen and the formaldehyde hydrogen atoms, which carry a small net positive charge. These results are given to illustrate the detailed information which can be extracted from the calculation, but they should be treated with caution, as minimal basis set calculations give rather poor charge distributions.

For smaller values of R, the overlap-dependent effects begin to dominate, and although there is still some variation in the electrostatic energy with θ, the reaction path is determined mainly by the exchange-repulsion term. The dominant effect is therefore a steric one. Detailed examination of the contributions to the exchange repulsion energy reveals that the O···O repulsion rapidly becomes large as θ decreases past 0°, while the two O···H repulsions increase as θ increases past 20°. The minimum at about 10° is thus the result of competition between these effects, exactly as one would expect.

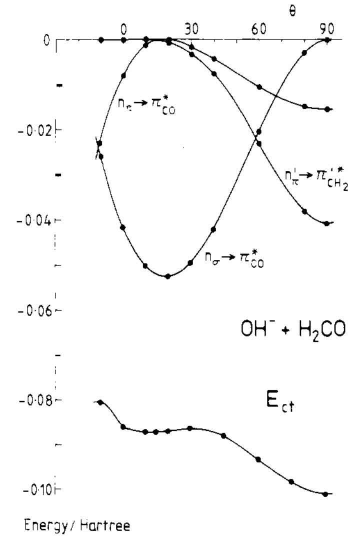

Figure 6. Important contributions to the charge-transfer energy for the reaction between hydroxide ion and formaldehyde. n_π and n'_π are the π-type lone-pair orbitals on OH^-, respectively parallel and perpendicular to the plane of Figure 1; $\pi'^*_{CH_2}$ is the antisymmetric combination of CH antibonding orbitals.

Equation II.18 shows that the charge-transfer term can be divided naturally into contributions, each arising from the interaction of an occupied orbital on one molecule with a virtual orbital on the other. The program has been written in such a way that these individual contributions can be listed, and the most important ones are shown in Figure 6. The interaction between

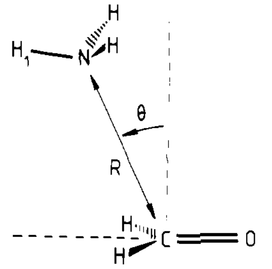

Figure 7. Symmetrical attack of ammonia on formaldehyde. The carbon atom lies on the C_3 axis of the ammonia molecule, and the atoms H_1, N, C, and O are coplanar.

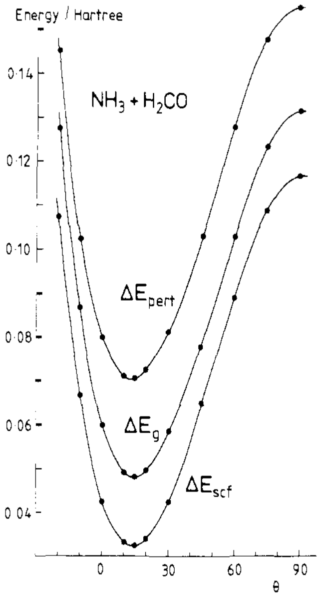

Figure 8. Perturbational energy ΔE_{pert} and variational energies ΔE_{scf} (calculated without ghost orbitals) and ΔE_g (calculated with ghost orbitals) for various directions of attack of ammonia on formaldehyde. N···C distance = 2 Å.

the OH^- σ lone-pair orbital n_σ and the formaldehyde π^*_{CO} orbital is a maximum, as one would expect, near $\theta = 20°$ and falls to zero when the hydroxide ion passes through either of the nodes in the π^*_{CO} orbital. However the $n_\pi \rightarrow \pi^*_{CO}$ contribution, which is zero near 20°, increases sharply in magnitude as θ becomes negative, while as θ approaches 90° the other OH^- π lone-pair orbital, n'_π, interacts strongly with the antisymmetric combination of CH antibonding orbitals, which we label $\pi'^*_{CH_2}$, following Jorgensen and Salem.[20]

It would therefore be invalid and misleading to approximate the total charge-transfer term by a single contribution, HOMO–LUMO or otherwise. Notice that the $n_\sigma \rightarrow \pi^*_{CO}$ term in Figure 6 mimics the total interaction energy (Figure 2) with striking accuracy for $R = 2$ Å and $-10° \leq \theta \leq 60°$. A calculation of this term alone might suggest that the directional effect could be explained in frontier-orbital terms, a conclusion which would evidently be wholly spurious.

V. Reaction of Ammonia with Formaldehyde

The ammonia reaction was studied with the geometry shown in Figure 7. Taking the distance R between the nitrogen and carbon atoms to be 2 Å, we obtain the curves shown in Figures 8 and 9. Again the perturbation and variational results are in excellent agreement, and Figure 9 shows that the pattern of the contributions to the perturbation energy is almost identical with that of the hydroxide reaction.

The fact that ammonia is a rather softer nucleophile than hydroxide, in Pearson's terminology,[21] might lead one to expect that the charge-transfer energy would be more important in the ammonia reaction and the electrostatic energy in the hydroxide one. The results given here provide no support for such a view. The detailed analysis of the charge-transfer contributions in the ammonia case, shown in Figure 10, confirms Bürgi's suggestion[19] that the major charge-transfer contribution arises from the mixing of the HOMO on NH_3, namely the lone-pair orbital, with the LUMO on H_2CO, the π^*_{CO} orbital. Because of the absence of n_π orbitals, the total charge-transfer term is smaller than that in the hydroxide case, and the HOMO–LUMO contribution is by far the largest at directions of attack near $\theta = 15°$. Because of the many small contributions, however, the variation of the charge-transfer energy with θ is still not dominated by the HOMO–LUMO contribution and does not have a strong influence on the direction of attack. The charge on the hydroxide ion seems to have no detectable effect on the behavior of the electrostatic energy, though it does increase the polarization energy to a small extent.

It should be emphasized that these results relate to an isolated pair of reacting molecules, and that the behavior of a pair of molecules surrounded by solvent might be very different. Unfortunately it would be very difficult to formulate the theory in the presence of solvent, but for the present we must conclude that attempts to explain hard/soft behavior in terms of competition

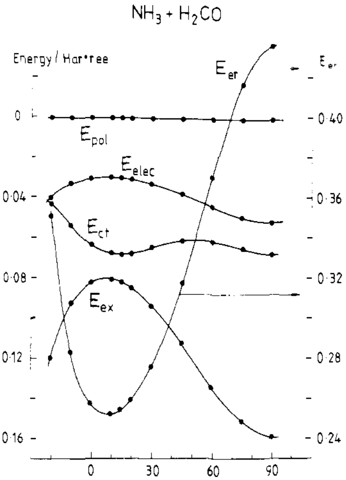

Figure 9. Contributions to the perturbational energy ΔE_{pert} for various directions of attack of ammonia on formaldehyde. N···C distance = 2 Å.

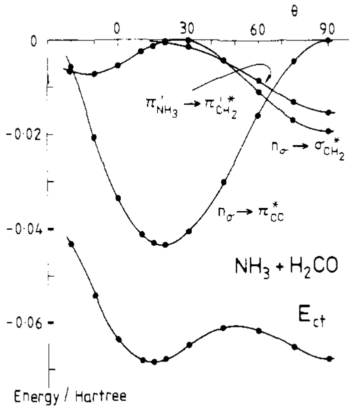

Figure 10. Important contributions to the charge-transfer energy for the reaction between ammonia and formaldehyde. n_σ is the σ lone pair on ammonia; π'_{NH_3} is one of the degenerate π-type N–H bonding orbitals on ammonia; $\sigma^*_{CH_2}$ is the symmetric combination of C–H antibonding orbitals.

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[20] W. L. Jorgensen and L. Salem, "The Organic Chemist's Book of Orbitals", Academic Press, New York and London, 1973.

[21] R. G. Pearson, *J. Am. Chem. Soc.*, **85**, 3533 (1963); *J. Chem. Educ.*, **45**, 581, 643 (1968).

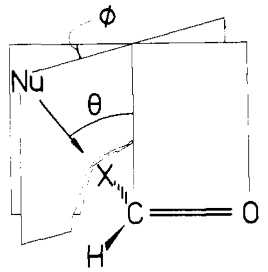

Figure 11. Geometry for attack of nucleophiles on carbonyl compounds. X = H, OH, NH_2, or O^-.

between charge-transfer and electrostatic effects cannot be substantiated by quantum-mechanical calculations.

VI. Nucleophilic Attack on Other Carbonyl Compounds

Baldwin[22] has proposed a model to explain the observed preferred direction of attack of nucleophiles on amides and other compounds. The model is not very explicit and is expressed in terms of resonance structures, but it can be paraphrased in the present terminology. The model considers only the position of the double bond in the resonance structure, and not the charge distribution, so it must be a charge-transfer model rather than an electrostatic one. Exchange repulsion is not considered in determining the direction of attack, but bulky substituents obstructing the preferred direction are supposed to inhibit reaction.

We can express the model in molecular-orbital terms as follows. We have seen that when $\theta \approx 15°$, as assumed by Baldwin, the only large charge-transfer contribution is the one arising from donation from the nucleophile n_σ orbital into the π^* orbital of the substrate. Defining the azimuthal angle φ as shown in Figure 11, we expect that for attack on ketones the charge-transfer energy will be greatest and the activation energy least when $\varphi = 0°$ (Figure 12a), because attack in any other direction will result in less favorable overlap between the donor orbital and the π^*_{CO} orbital. If X is OH or NH_2, however, the π^* orbital extends over the O or N atom (Figure 12b), though with a smaller coefficient than on the carbonyl oxygen, and the most favorable direction of attack will be for a positive value of φ. Moreover the π^* orbital will have a smaller coefficient at the X atom when X = O than when X = N, because oxygen is more electronegative than nitrogen and so has larger coefficients in the bonding orbitals, and consequently the optimum value of φ will be somewhat smaller in this case. Finally, if X is O^-, so that the substrate is a carboxylate anion, the π^* orbital is symmetrical (Figure 12c) and the favored direction of attack is at $\varphi = 60°$.

All this is little more than a translation of Baldwin's argument into molecular-orbital language, and the conclusions are essentially unchanged. Let us now see whether the SCF perturbation theory supports the argument.

We have carried out calculations on model systems consisting of formaldehyde, formic acid, formamide, and formate ion attacked by hydroxide ion. Formic acid is here a model for esters, and although the model reaction is an implausible one the results should be valid for the ester case. Similarly it would be more plausible to use an uncharged nucleophile for the reaction with carboxylate ion, but it seemed more satisfactory to use the same nucleophile throughout.

We concentrate our attention on φ, and have performed a series of calculations with $\theta = 15°$, $R = 2$ Å, and φ in the range 0–120°. In all cases the perturbation calculations were in excellent agreement with variational SCF calculations as to the variation of the interaction energy with φ, as Figure 13 shows. Moreover the preferred direction is in full agreement with the predictions of Baldwin's model. The details are given in Figure 14, and we see immediately that for formaldehyde the charge-transfer and electrostatic energies are independent of φ over the range shown. The form of the exchange-repulsion and exchange terms will of course depend on the nature of any substituents. Thus there is nothing particularly significant about the $\varphi = 0°$ direction for ketones; it will usually be favored sterically, as it is here, but we should not expect reaction to be seriously inhibited if bulky substituents on one side of the carbon atom force an attack away from $\varphi = 0°$.

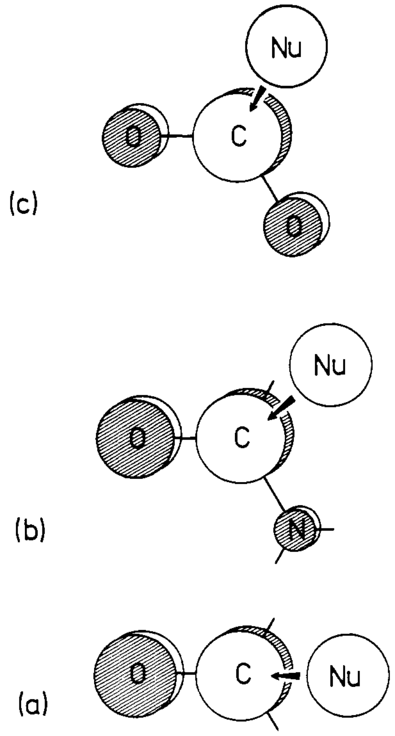

Figure 12. Orbitals involved in the major charge-transfer contribution in nucleophilic attack on (a) ketones, (b) amides, and (c) carboxylate ions.

The position is quite different in the other three cases, which however are similar to each other. There is now a marked variation of the charge-transfer and electrostatic energies with φ, and these two effects virtually dictate the direction of attack. If the substituents are such as to obstruct this direction, they will inhibit the reaction. Examination of the individual charge-transfer contributions shows that the $n \rightarrow \pi^*_{CO}$ term is by far the largest, though rarely more than half the total, and that it decreases sharply in magnitude as φ is changed from its optimum value. The total of the remaining contributions is by no means independent of φ, but it does not vary as much as the frontier-orbital term, which therefore can reasonably be regarded as determining the optimum direction of attack.

We conclude that Baldwin's model is essentially correct, though he attaches undue significance to the idea of attack in the direction of the double bond, and that the process can be usefully understood in frontier-orbital terms. At the same time it is important to stress that there are other significant effects to consider, notably the electrostatic contribution.

VII. Conclusions

We have shown that Basilevsky and Berenfeld's self-consistent-field perturbation theory[7] can be implemented satisfactorily within the framework of the GAUSSIAN-70 program, that it gives results which are in excellent agreement with those obtained by using supermolecule SCF calculations, and that the results can be analyzed in considerable detail if required. In particular, the pairs of orbitals which contribute most significantly to the charge-transfer or resonance energy can be indentified. The method is therefore complementary to Morokuma's,[12] which is not limited by the approximations of perturbation theory but does not yield such detailed information. The perturbation theory diverges if the interaction is too strong, but the offending term or terms can be readily identified and their contributions recalculated by using an approximation to degenerate perturbation theory. In any case the region of configuration space which can

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(22) J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 738–741 (1976).

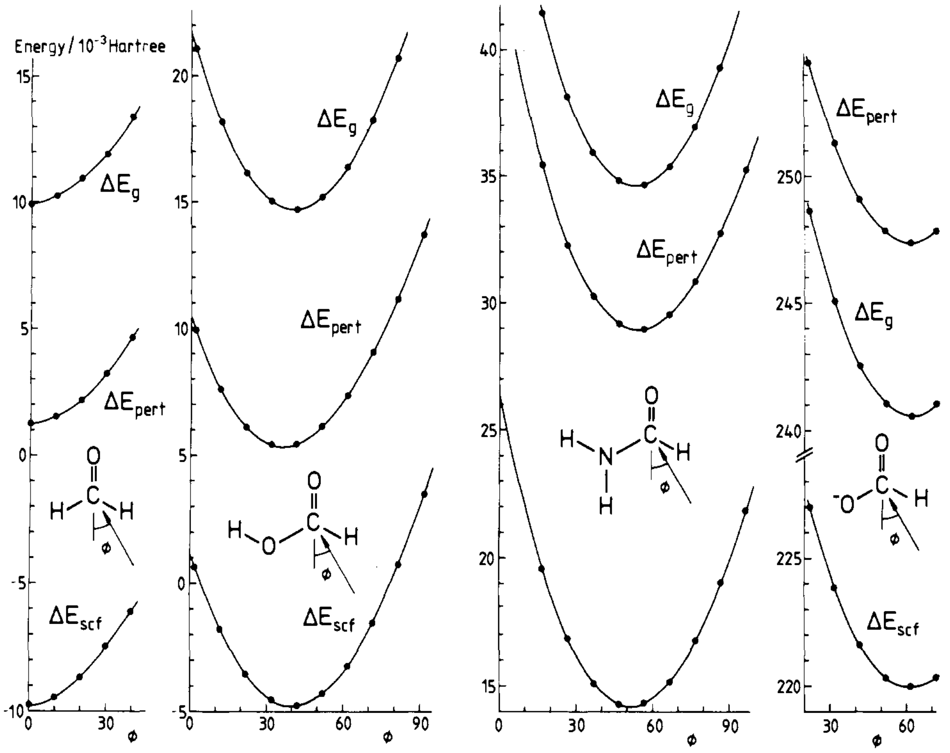

Figure 13. Energy of interaction of hydroxide ion with (a) formaldehyde, (b) formic acid, (c) formamide, and (d) formate ion, as a function of φ. Geometry as in Figure 11; Nu$\cdots$C distance = 2 Å, θ = 15°.

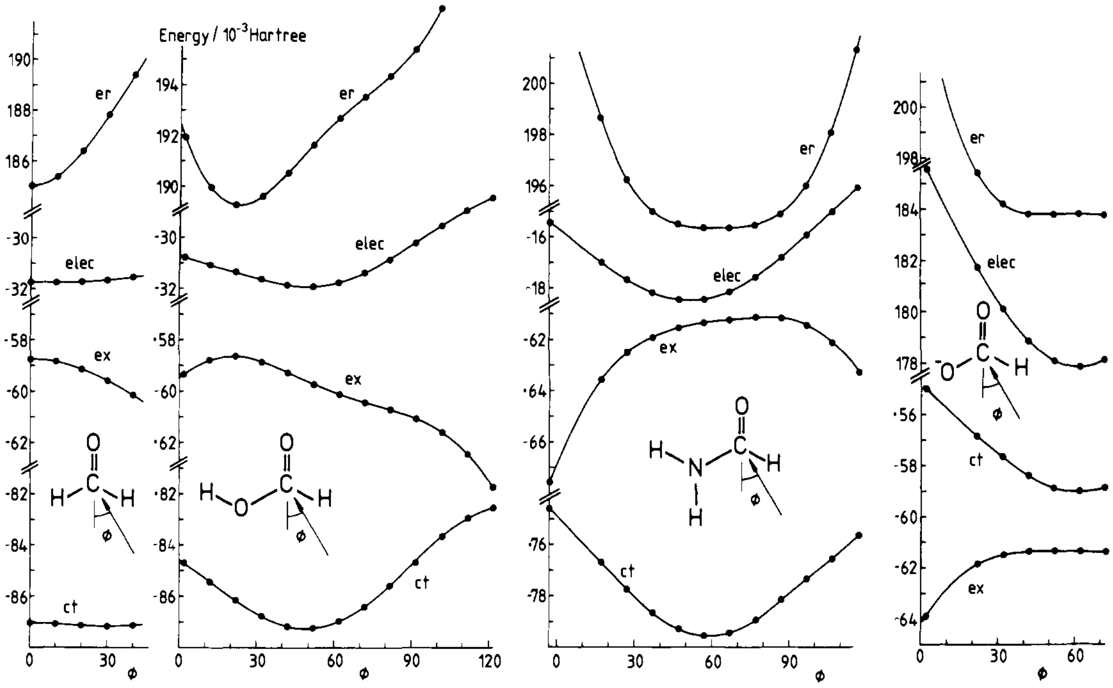

Figure 14. Contributions to the perturbational energy for reaction of hydroxide ion with (a) formaldehyde, (b) formic acid, (c) formamide, and (d) formate ion, as functions of φ. Geometry as in Figure 11; Nu$\cdots$C distance = 2 Å, θ = 15°.

be studied without interference from divergence difficulties is quite large enough for useful conclusions to be drawn. We find also that optimization of molecular geometries, while important in the study of the final stages of a reaction, is not essential in the earlier stages. Our calculations agree in their predictions both with other methods of calculation and with experiment, but we are able to give a more detailed interpretation of the results, which does not always agree with views previously expressed.

We conclude that this is a useful way of studying the nature of the interaction between reacting molecules, and especially of examining the merits and deficiencies of frontier-orbital theory and similar approximate models.

Acknowledgment. We are indebted to Dr. I. Fleming for numerous valuable discussions. R.W.E. thanks the SRC for a research studentship.