and fluorine. This again is understandable, since the total correlation energy is expected to be larger in a neutral molecule than in the corresponding cation.

Conclusions

The following general conclusions may be drawn from this work: (1) The molecular orbital configurations and geometrical shapes of the smaller neutral molecules considered are correctly given by the rules formulated by Walsh.[19,23] Most of these results are now confirmed experimentally.[10,11] (2) Positive ions are found to have states and structures which are similar to those of the isoelectronic neutral systems. However, some opening out of bond angles is predicted by the theory. (3) The theory indicates that the lowest triplet states of the saturated molecules do not exist as tightly bound species but rather are loose intermolecular complexes between smaller fragments. The same applies to the higher valency compounds CH_5, NH_4, H_3O, and H_2F.

Acknowledgments. The initial version of the complex self-consistent-field routines was written by Dr. D. Miller. Useful discussions with Mr. J. B. Lisle are acknowledged. This research was supported in part by National Science Foundation Grant No. GP25617.

Molecular Orbital Studies on Bifunctional Catalysis of Glucose Mutarotation. The Hydrogen Bond with 2-Pyridone[1]

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Abstract: The CNDO/2 MO method was used to study the double hydrogen bond between 2-pyridone and the portion of the glucose molecule involved in the mutarotation reaction. A correction was applied to the energy curve to account for kinetic energy constraints. The calculations indicate that the double hydrogen bond is stronger than the sum of the two separate single hydrogen bonds. The reasons appear to involve electron delocalization and a difference in the number of degrees of freedom of kinetic energy lost per hydrogen bond. In addition, it was found that the electronic rearrangements that characterized the actual ring-opening reaction are initiated with the formation of the hydrogen bond.

The concerted action of two or more functional groups is generally recognized as an important factor in enzyme catalysis. This was first suggested by Swain and Brown[2] on the basis of their study of the mutarotation of tetramethylglucose. In recent years the suggestion has received considerable support from structural and kinetic studies of enzymes. The current investigations are part of an effort to learn more about the basis for the rate enhancement in the model reaction.

A Hückel MO study of a series of bifunctional catalysts[3] led to the conclusion that electronic coupling between the functional groups is an important factor. This is in qualitative agreement with the conclusion reached by Rony[4] on the basis of measurements of activation parameters. Rony[5] later suggested electronic coupling as a generally necessary condition for concerted reactions.

The first stage of the interaction must involve a double hydrogen-bond (H bond) formation between catalyst and substrate. This paper reports the results of molecular orbital calculations, in the CNDO/2 approximation,[6,7] on the hydrogen bonding of glucose with 2-pyridone. The extended Hückel procedure[8] was also tried but was not suitable.

Cooperativity effects appear to cause a decrease in the lengths of the H bonds and an increase in the stabilizing energy.

Calculations

Calculations were performed on the IBM 360/75 of the Triangle Universities Computing Center. Intermediate numbers were carried in double precision for all molecular orbital calculations.

(1) Molecular Orbital Procedure. The CNDO/2 calculations were performed with QCPE program CNDOTWO.[9] The program was modified to suit local input–output requirements and to facilitate changing dimension statements. A further modification was the use of an eigenvalue subroutine[10] based on the Q-R algorithm.[11] Parameters used were those of Pople and Segal.[7] Except for hydrogen, the orbital exponents were those given by Slater's[12] rules. An exponent of 1.2 was used[13] for hydrogen 1s.

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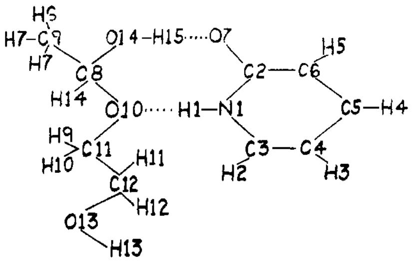

Figure 1. Structure of the doubly H-bonded pair, showing the truncated glucose structure and the numbering system.

Extended Hückel calculations were done with QCPE program EXTHUC[14] modified as described above for CNDOTWO. Parameters were those originally recommended by Hoffmann.[8,15–17] Orbital exponents were the same as for CNDOTWO.

(2) Coordinates. Atomic coordinates were calculated with QCPE program PROXYZ.[18] Bond lengths and angles were obtained from Sutton[19] and references cited there.

Specifically, data for 2-pyridone were based on the studies of Penfold,[20] except that the structure was taken as planar. Although Penfold's data show small deviations from planarity, the deviations are within the estimated experimental error. Moreover, both extended Hückel and CNDO calculations give a slight preference to a planar structure.

Bond lengths and angles for α-glucose were taken from the data of McDonald and Beevers[21] except that O–H distances were taken as 0.99 Å. The current study concerns that portion of the glucose molecule which enters into the ring-opening and -closing reactions. Atoms remote from this "reaction center" are not likely to have a significant effect. A possible exception is the $-CH_2OH$ side chain, which approaches the 2-pyridone molecule in the H-bonded complex. Accordingly, a truncated structure (GT) (Figure 1) was used. The calculations (extended Hückel and CNDO) indicate that the only significant changes involve atoms C_8, O_{10}, O_{14}, H_{14}, and H_{15} of the GT structure. Trends shown by extended Hückel calculations using the full and truncated structures were parallel to each other.

Auxiliary programs were written for rotating and translating one portion of a molecule relative to another, using standard trigonometric and geometric relationships.

(3) The H-Bonded Structures. In order to evaluate the effects of cooperativity on the doubly H-bonded structure, it is necessary to know something about the singly bonded structures. Geometries were chosen, with the help of Corey–Pauling–Koltun Ealing space-filling molecular models, to minimize interactions between the two components other than the H bond under study. The H bonds were assumed to be linear. For the O—H···O bond, the geometry was defined by the following conditions: (a) O_{14}, H_{15}, and O_7 collinear; (b) 2-pyridone coplanar with atoms O_{10}, O_{14}, and H_{15}; (c) the O_{14}–O_7–C_2 angle 110°. The minimum energy was sought with respect to the O_7–O_{14} distance, keeping all other distances and all angles fixed.

For the N—H···O bond, the geometry was fixed by the following conditions: (a) O_{10}, H_1, and N_1 collinear; (b) atoms O_{10}, H_1, and N_1 coplanar with atoms C_8, O_{10}, C_{11}; (c) the O_{10}–N_1 line bisecting the C_8–O_{10}–C_{11} angle; (d) the pyridone plane at right angles to the C_8–O_{10}–C_{11} plane, with O_7 and O_{14} in the same hemisphere. The minimum energy was sought with respect to the N_1–O_{10} distance, keeping all other distances and all angles fixed.

For the doubly H-bonded structure, conditions used were: (a) O_{14}, H_{15}, and O_7 collinear; (b) O_{10}, H_1, and N_1 collinear; (c) O_{10}, O_{14}, and H_{15} coplanar with the pyridone molecule. The minimum energy was sought with respect to the O_{14}–O_7 distance. For each new O_{14}–O_7 distance specified, it was necessary to rotate the pyridone molecule slightly to satisfy condition b. Note that given conditions a, b, and c and the rigidity of the participating components, the O_{14}–O_7 and O_{10}–N_1 distances cannot be simultaneously specified.

In each case the energy minimum was located by a graphical interpolation procedure to a precision of about ±0.005 Å.

(4) Analysis of the Wave Functions. The coefficients obtained from the SCF–CNDO iteration were used directly. These may be interpreted[22] as approximations to coefficients in a symmetrically orthogonalized[23,24] basis set. The process of symmetric orthogonalization produces a basis set, the Löwdin basis, which retains maximum similarity to the original Slater orbitals. The functions of such a set may be considered to be associated with mutually orthogonal neighborhoods of phase space, each centered about a particular atom. The matrix of the transformation between the Slater and Löwdin basis is $S^{1/2}$, where S is the overlap matrix of the Slater basis. In the limit of large interatomic distances, the Slater and Löwdin bases become identical. In the present series of calculations, the only overlaps that vary are those between atoms on the two different components. Since these are negligible in all cases, the results of all of these calculations may be taken as referring to the same symmetrically orthogonalized (and normalized) basis set. This property is needed in the discussion of MO correlations (paragraph c below).

(a) Charges. Using the CNDO coefficients as approximations to coefficients relative to a Löwdin basis, the charges may be computed according to the prescription of Coulson and Longuet-Higgins.[23,25] Letting $\{\Psi_j\}$ be the set of molecular orbitals and $\{\phi_\mu\}$ be the atomic orbitals of the Löwdin basis

$$\Psi_j = \sum_{\mu=1}^{n} c_{j\mu}\phi_\mu \tag{1}$$

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The "atomic orbital electron density" may be defined as

$$q_\mu = 2\sum_j c_{j\mu}^2 \qquad (2)$$

and the total electron density on atom A is

$$q_A = \sum_{\mu\epsilon(A)} q_\mu \qquad (3)$$

where (A) is the set of atomic orbitals centered on atom A.

The CNDOTWO program as received transforms the CNDO coefficients back to the Slater basis and performs a Mulliken population analysis.[26] This calculation was retained for comparison. A deficiency of the Mulliken analysis is that it assumes the shared charge between two atoms to be symmetrically distributed.[26,27]

(b) Bond Indices. Electron delocalization has been examined with the use of long-range bond orders[28,29] and bond indices.[29-31] Wilberg[30] defines the bond index $W_{\mu\nu}$ as the square of the bond order, $p_{\mu\nu} = 2\Sigma_{j\text{occ}} c_{\mu j} c_{\nu j}$. Letting ϕ_μ be an AO centered on atom A, Trindle and Sinanoglu[31] interpret $W_{\mu B} = \Sigma_{\nu\epsilon(B)} W_{\mu\nu}$ as the charge shared between ϕ_μ and atom B. Similarly, the total charge shared between atoms A and B may be taken as

$$W_{AB} = \sum_{\mu\epsilon(A)}\sum_{\nu\epsilon(B)} W_{\mu\nu} \qquad (4)$$

This quantity will be called the atom–atom bond index.

(c) MO Correlations. Separate calculations were made for 2-pyridone and the truncated glucose structures. The separate MO coefficient vectors were combined into a single matrix, taken to be the coefficient matrix of a pyridone–GT pair with zero interaction. These "zero-interaction" MO's, $\{\chi_i\}$, were used as a basis set in which to express the orbitals Ψ_j of an H-bonded pair

$$\Psi_j = \sum_i T_{ji}\chi_i \qquad (5)$$

Since the $\{\Psi_j\}$ and $\{\chi_i\}$ are obtained with reference to the same orthonormal basis, T_{ji} is the simple dot product of the coefficient vectors.

When the O_{14}–O_7 distance was taken as 20 Å, the **T** matrix of eq 5 was diagonal, with the $T_{ii} = \pm 1$. This "H-bonded" pair could therefore be used equivalently as a "zero-interaction" structure.

In each case, the occupied MO's of the interacting pair could be expressed as linear combinations of the *occupied* zero-interaction MO's. For a given Ψ_j, the fractional pyridone and glucose contributions were defined as

$$F_{jP} = 2\sum_{i\epsilon(P)} T_{ji_P}^2 \qquad (6a)$$

$$F_{jG} = 2\sum_{i\epsilon(G)} T_{j,i_G}^2 \qquad (6b)$$

where the summations run over the orbitals (occupied) of pyridone and GT, respectively. The degree of interaction can be summarized by defining a "correlation index"

$$R_j = F_{jP}F_{jG} \qquad (7)$$

This index varies between zero for no interaction and one for maximum interaction, where $F_{jP} = F_{jG} = 1.0$.

(5) Kinetic Energy Correction. As two molecules are brought together under the influence of an attractive potential, the restrictions on relative motion lead to an increase in kinetic energy. The equilibrium distance is the result of a balance between the attractive and repulsive electronic interactions (which may be classified as, for example, by Coulson[32]), the nuclear repulsions, and the increase in nuclear kinetic energy. Within the context of the Born–Oppenheimer approximation, the nuclear contributions may be computed separately and added at the end. The CNDO procedure takes explicit account of the nuclear repulsions but, in common with other molecular orbital procedures, neglects any change in nuclear kinetic energy. While this neglect is quite reasonable for the purpose of discussions of normal covalent bonds, the force constants of H bonds are several orders of magnitude lower, and corrections of 1–2 kcal/mol become significant. To the extent that molecular orbital calculations are of value in understanding H bonds, it would seem that more appropriate estimates of lengths and energies are obtained by moving out along the calculated energy curve a distance of $nkT/2$, where k is the Boltzmann constant, T is absolute temperature, and n is the number of degrees of freedom of kinetic energy lost. A molecule which complexes to another by a single hydrogen bond may retain free rotation about one axis, and loses five degrees of freedom (three translational and two rotational). A molecule which forms two H bonds to another loses six degrees of freedom.

Such a correction applied to published H-bond energy curves computed by CNDO/2 procedures[33-36] significantly improves agreement with experimental observation.[37] Lippincott and Schroeder[38] used a kinetic energy correction in the application of their empirical H-bond potential function.

Results and Discussion

(1) Extended Hückel Calculations. The extended Hückel calculations for the O_7–O_{14} single H bond showed a minimum at 2.91 Å of 3.6 kcal/mol (uncorrected for kinetic energy). No energy minima were found for the N_1–O_{10} single H bond or for the doubly H-bonded structure. These results are similar to those found by other authors.[33-36] A probable source of this qualitative disagreement with experiment is the failure of neglected repulsion terms to balance.[39]

The remaining discussion is based on the results of the CNDO calculations.

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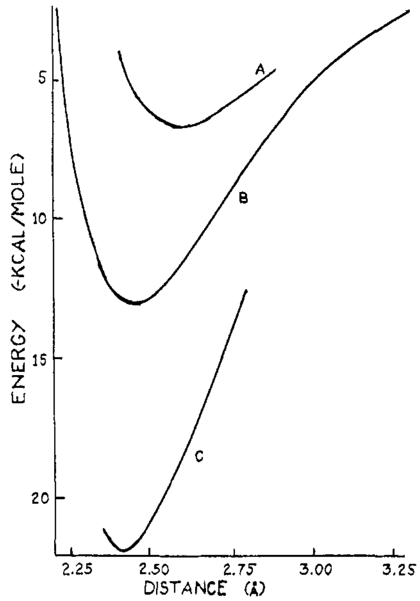


Figure 2. CNDO/2 energy curve for 2-pyridone–GT H-bonded pairs. Zero of energy is taken as the energy at infinite separation: A, single N_1–O_{10} H bond; B, single O_7–O_{14} H bond; C, the O_7–O_{14} distance in the doubly H-bonded pair.

(2) H-Bond Lengths and Stabilization Energies. The energy curves for the three types of complexes studied are shown in Figure 2. Equilibrium H-bond lengths and energies, before and after application of the kinetic energy correction, are listed in Table I.

Table I. H-Bond Lengths (Å) and Stabilization Energies (kcal/mol)

	Uncorrected		Corrected[a]	
	Energy	Length	Energy	Length
		Single		
O_7–O_{14}	12.78	2.450	11.29	2.600
N_1–O_{10}	6.52	2.585	5.03	2.820
		Double		
O_7–O_{14}	21.49	2.410	19.70	2.540
N_1–O_{10}		2.580		2.710

[a] Kinetic energy correction of $^5/_2kT$ for single H bonds and $^6/_2kT$ for double, calculated for T = 300°K.

The corrected H-bond lengths for the single O···O and N···O bonds are in good agreement with expected lengths.[40] The stabilization energies seem somewhat high, although they are of reasonable magnitude and, more important, in reasonable relation to each other.

As mentioned in the previous section, the relation between the lengths of the two H bonds could not be made a constraint in the calculation of the geometry of the doubly H-bonded structure. Nevertheless, the relation was very close to the relation between the corresponding singly H-bonded structures. This is, of course, because geometries of the two components match well enough to form the two H bonds without appreciable strain.

There are, however, striking differences between the behavior of the doubly H-bonded complex and of the singly bonded complexes. For the doubly bonded complex, the equilibrium bond lengths are shorter, the energy curve is steeper, and the stabilization energy is greater than the sum of the energies of the two separate single bonds. This would be true even if the energy for the doubly bonded structure were corrected for the loss of *ten* degrees of freedom. This implies that two factors contribute to the shortening of the H bonds. The first is the fact that two H bonds are formed with kinetic energy constraints only slightly greater than for the formation of one. The second is an electronic cooperativity (delocalization) effect between the two H bonds. The cooperativity is discussed below in more detail.

(3) Charge Distribution. The nitrogen and oxygen atoms start off with strong negative charges, with the associated hydrogens strongly positive (Table II).

Table II. Atomic Charges in Doubly H-Bonded Pyridone–GT Pairs[a]

	O_7–O_{14} distance, Å			
Atom	20.0	2.80	2.54	2.41
H_1	+0.131	+0.155	+0.177	+0.197
H_{14}	−0.066	−0.073	−0.079	−0.084
H_{15}	+0.152	+0.196	+0.224	+0.246
N_1	−0.165	−0.175	−0.189	−0.201
C_2	+0.364	+0.374	+0.382	+0.389
C_3	+0.161	+0.165	+0.169	+0.172
O_7	−0.393	−0.409	−0.415	−0.418
C_8	+0.354	+0.359	+0.363	+0.366
O_{10}	−0.249	−0.268	−0.274	−0.278
O_{14}	−0.269	−0.300	−0.334	−0.361

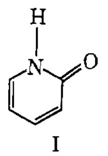
[a] Charges are shown for atoms whose charges are altered by at least 0.01.

During the course of H-bond formation, the magnitudes of the charges increase as the electron density appears to move away from the hydrogen atom toward the two electronegative atoms. This change, which is quite marked at the equilibrium bond distance, is already in evidence at larger H-bond distances (Table II). The *total* electron density of the N—H···O bond is unchanged, while that of the O—H···O bond is slightly increased. These results are in accord with those of other authors[35,36] and with the general observation that the dipole moment of a hydrogen-bonded complex is greater than would be expected on the basis of the properties of the separate molecules.

An examination was also made of the charges calculated from a Mulliken population analysis[26] using the coefficients for the Slater-type orbital basis. Although most of the charge magnitudes given by this calculation were considerably greater, the same patterns are shown.

(4) Bond Indices. Data are given in Tables III and IV. As discussed in the previous section, W_{AB} defined by eq 4 may be taken as a measure of the electron density shared by atoms A and B.

Within the pyridone ring, a definite pattern of bond alternation is indicated. This is in agreement with the simple π-electron Hückel calculation and clearly suggests the classical organic structure I.



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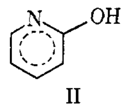

II

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Table III. Nearest-Neighbor Atom–Atom Bond Indices in Doubly H-Bonded Pyridone–GT Pairs

	O_7–O_{14} distance, Å			
Atom pair	20.0	2.80	2.54	2.41
N_1–H_1	0.948	0.931	0.907	0.884
O_{10}–H_1	0.0	0.010	0.027	0.045
O_{14}–H_{15}	0.952	0.912	0.863	0.820
O_7–H_{15}	0.0	0.026	0.052	0.097
C_2–O_7	1.648	1.617	1.587	1.561
N_1–C_2	1.051	1.066	1.081	1.094
N_1–C_3	1.232	1.238	1.244	1.250
C_3–C_4	1.648	1.641	1.635	1.629
C_4–C_5	1.207	1.213	1.220	1.225
C_5–C_6	1.705	1.696	1.687	1.680
C_2–C_6	1.137	1.145	1.154	1.160
C_8–O_{14}	1.020	1.035	1.046	1.055
C_8–C_{10}	0.932	0.919	0.909	0.899

Table IV. Some Long-Range Atom–Atom Bond Indices in Doubly H-Bonded Pyridone- GT Pairs

	O_7–O_{14} distance, Å			
Atom pair	20.0	2.80	2.54	2.41
N_1–O_{10}	0.000	0.007	0.018	0.028
O_7–O_{14}	0.000	0.016	0.036	0.051
O_7–C_6	0.042	0.043	0.044	0.044
N_1–O_7	0.122	0.120	0.118	0.115
N_1–C_4	0.060	0.058	0.055	0.053
N_1–C_5	0.045	0.048	0.050	0.053
N_1–C_6	0.014	0.013	0.012	0.011
C_2–C_3	0.003	0.003	0.003	0.003
C_2–C_4	0.031	0.034	0.037	0.039
C_2–C_5	0.012	0.013	0.014	0.014
O_{10}–O_{14}	0.038	0.039	0.040	0.040
N_1–O_{14}	0.000	0.000	0.001	0.001
C_2–O_{14}	0.000	0.001	0.001	0.002
C_6–O_{14}	0.000	0.000	0.001	0.001
O_7–C_8	0.000	0.000	0.000	0.001

The low bond index for the C_8–O_{10} bond is interesting in view of the suggestion of Pullman and Pullman[41] that electron deficiency is a characteristic of bonds whose cleavage is easily catalyzed.

The following changes in bond indices are expected to be associated with the actual ring opening reaction: (a) those of the pyridone ring are expected to become more equal as its structure moves toward structure II, (b) bond indices for the C_8–O_{10}, N_1–H_1, and O_{14}–H_{15} bonds are expected to *decrease* as these bonds are broken, (c) the C_2–O_7 bond index is expected to *decrease* as this bond loses part of its double bond character, (d) the indices for O_{10}–H_1 and O_7–H_{15} are expected to *increase* as these bonds form, and (e) the C_8–O_{14} index is expected to *increase* as this bond takes on double bond character. As shown in Tables III and IV, all of these changes are initiated at the onset of H-bond formation and are already moderately advanced at the equilibrium bond distance. It is therefore not strictly correct to say that the ring-opening reaction is *preceded* by H-bond formation. The reaction itself begins with the formation of the H bond. On this basis, one is tempted to speculate that examination of the potential surface for the movement of the protons will show the equilibrium O_{14}–H_{15} and N_1-H_1 distances to be increased more than is usually the case. Such calculations should involve minimization of energy simultaneously with respect to the positions of the two hydrogens and the lengths of the two H bonds.

At the equilibrium H-bond distance, the bond indices for the pairs N_1–O_{10} and O_7–O_{14} are of the order of magnitude of those for nonneighbor indices within the pyridone ring. Indices for C_2 or C_6 with O_{14} and O_{10} (Table IV) are small but nonzero.

(5) Molecular Orbital Interactions. Table V shows the correlation indices, defined by eq 7, for those orbitals which attain at least the value 0.9 for some H-bond distance. A value of 0.9 means that each component contributes between one-third and two-thirds of the electron density to that molecular orbital. The lowest energy orbital and the highest energy occupied orbital are also shown.

Table V. Correlation Indices (Eq 7) for Doubly H-Bonded Pyridone–GT Pairs

	O_7–O_{14} distance, Å		
Orbital[a]	2.80	2.54	2.41
1	0.139	0.322	0.474
4	0.726	0.862	0.930
5	0.759	0.981	0.986
17	0.738	0.998	0.958
18	0.856	0.963	0.802
22	0.703	0.888	0.910
23	0.646	0.926	0.992
25	0.513	0.926	0.942
26	0.771	0.980	0.988
29[b]	0.374	0.781	0.585
30[b]	0.062	0.996	0.992
32	0.931	0.980	0.979
33	0.311	0.820	0.988
38	0.982	0.899	0.787
39	0.990	0.970	0.948
40[b]	0.000	0.000	0.001

[a] Numbered in order of increasing energy. Orbital 40 is the highest occupied orbital. [b] These are pure pyridone π orbitals in the zero-interaction set.

The highest occupied orbital is a pyridone π orbital. It shows no appreciable interaction at any distance.

The strongest interactions at the greater distances involve the highest σ orbitals of the two molecules. At smaller distances, however, strong interactions appear over the whole spectrum of energy levels.

Levels 29 and 30 involve substantial mixing of pyridone π orbitals with the GT system. These are pure pyridone π orbitals in the zero-interaction set. During H-bond formation, they mix with each other and with orbitals of the GT system. At an O_7–O_{14} distance of 2.6 Å, this interaction has already become substantial.

(6) Implications. The experimental and theoretical evidence of the "softness" of the hydrogen bond has been reviewed elsewhere.[38,42] It was suggested that enzymes might enhance the rate of proton transfer across H bonds by providing other points of interaction which would allow the H-bond distances to be shortened.

In the reaction between 2-pyridone and glucose, it appears that the electronic cooperativity between the two H bonds makes the potential energy curve steeper

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[41] B. Pullman and A. Pullman, "Quantum Biochemistry," Wiley, New York, N. Y., 1963, Chapter 17.

[42] H. J. Gold, *Int. J. Quantum Chem.*, 4, 353 (1971).

than the sum of the two individual curves and draws the two molecules more closely together than would otherwise be the case. The closeness of approach and the degree of electronic interaction is further enhanced by the reduction in the number of degrees of freedom of kinetic energy per H bond that must be accounted for. This is especially significant since the interaction initiates the actual ring-opening reaction.

Molecular Orbital and Mapping Study of the Allowed Diels–Alder Reactions of Furan, Thiophene, and Thiophene Dioxide

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Abstract: Concerted Diels–Alder addition to thiophene, thiophene dioxide, and furan is allowed in the sense that the symmetry species of the set of occupied orbitals is maintained through the reaction. To account for experimentally observed differences in reactivity of these molecules, a more detailed appreciation of the reaction potential is required. With the aid of qualitative ideas from perturbation theory, the observed order of reactivity is rationalized.

The symmetry arguments of Woodward and Hoffmann[2] provide a reliable guide to forbidden processes; still, the statement that a given reaction path is not barred by fundamental symmetry laws does not guarantee that the reaction path will be followed, for two reasons. First, alternate concerted reactions may be possible; for example, both cis–cis and trans–trans Cope rearrangements are allowed, but only the easier latter route is observed.[3] Second, the desired products may simply be less stable thermodynamically than the reactants; equilibration would be rapid, since reactants and products interconvert readily, but would favor the stabler species.

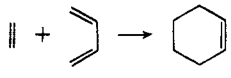
An understanding of alternate allowed reaction pathways, or prediction of the position of a certain equilibrium, requires some appreciation of the energy surface for the reaction. Practical considerations seem to rule out direct point-by-point computation of the energy surface, except in crude approximation, or for the simplest systems.[4] However, qualitative and semiquantitative arguments developed recently[5] allow an understanding of many of the important features of reaction surfaces. In this report we employ some of the methods of Woodward and Hoffmann, Pearson, and Hoffmann to study the relative reactivities of furan, thiophene, and thiophene dioxide toward dienophiles.

Furan's Diels–Alder reactivity[6] has received considerable attention: the reaction is facile, with a pronounced reversibility. Substituents with a −M effect tend to inhibit the Diels–Alder addition, though powerful dienophiles will add successfully. Thiophene, in contrast, does not act as a diene;[6] its chemistry is that of an aromatic system, including Friedel–Crafts alkylation, bromination, etc. The concerted Diels–Alder reaction is not observed.

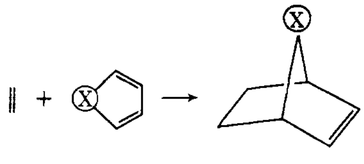
Thiophene dioxide participates in Diels–Alder reactions either as a diene or as a dienophile; it tends to dimerize by a Diels–Alder route. As an electron-deficient diene, it is not highly reactive; the standard dienophile maleic anhydride is rebuffed, although the more powerful reagent diethyl acetylenedicarboxylate is accepted. Bailey and Cummins[6] assert that "resonance stabilization" is lacking in thiophene dioxide, since it is more reactive than analogous open-chain sulfones.

The Influence of Heteroatoms on the Diels–Alder Addition

The simplest prototype of the (1,4) Diels–Alder condensation is the combination of ethylene with butadiene



The Diels–Alder condensation of heterocyclic dienes seems closely related to the simple example mentioned



Therefore, let us consider the heteroatom to exert a perturbation on the diene fragment. Usual discussions

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[1] (a) University of Virginia. (b) A portion of this work was performed under the auspices of the U. S. Atomic Energy Commission during the tenure of a Center for Educational Affairs Associateship at the Argonne National Laboratory.

[2] R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlage Chemie, Weinheim, Germany, 1970.

[3] J. E. Baldwin and M. S. Kaplan, *Chem. Commun.*, 1354 (1969).

[4] But see papers by Wahl, *et al.*, for example, A. C. Wahl and G. Das, *Advan. Quantum Chem.*, **5**, 261 (1970).

[5] R. G. Pearson, *Theor. Chem. Acta*, **16**, 107 (1970); *J. Amer. Chem. Soc.*, **91**, 1252, 4947 (1969).

[6] Thiophene, S. Gronowitz, in *Advan. Heterocycl. Chem.*, **1**, 2 (1963); thiophene dioxide, W. J. Bailey and E. W. Cummins, *J. Amer. Chem. Soc.*, **76**, 1940 (1954); furan, P. Bosshard and C. M. Eugster, *Advan. Heterocycl. Chem.*, **7**, 378 (1966).