

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 Hoffmann² 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 semi-quantitative arguments developed recently⁵ 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.

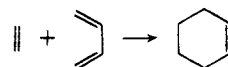
Furan's Diels–Alder reactivity⁶ has received considerable attention: the reaction is facile, with a pro-

nounced 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.

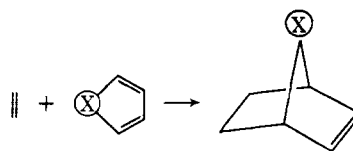
Thiophene dioxide participates in Diels–Alder reactions either as a diene or as a dienophile; it tends to dimerize by a Diels–Alder route. As an electron-deficient diene, it is not highly reactive; the standard dienophile maleic anhydride is rebuffed, although the more powerful reagent diethyl acetylenedicarboxylate is accepted. Bailey and Cummins⁶ 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

(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," Verlag 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).

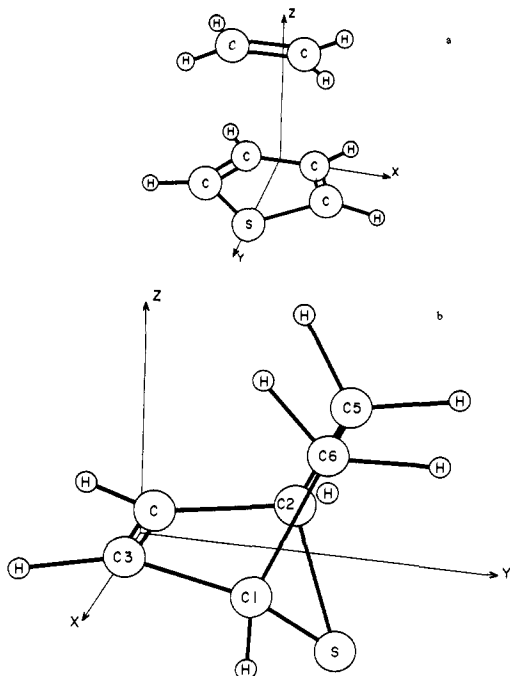


Figure 1. (a) Assumed approach of the prototypic dienophile ethylene to a diene, thiophene. (b) Side view of the putative Diels-Alder adduct, 7-thiabicyclo[2.2.1]hept-2-ene, of ethylene with thiophene.

of Diels-Alder additions⁷ stress the role of the π orbitals of the reactants; the butadiene MO's are of symmetry species $S_\pi + A_\pi$, where the label S or A denotes symmetric or antisymmetric, respectively, with respect to a plane perpendicular to the σ plane and containing the twofold axis of the diene.

In the course of the Diels-Alder condensation, ethylene approaches in such a way that its occupied π MO is classified as S with respect to this plane (Figure 1). Two σ bonds are formed primarily from the A_π butadiene MO and S ethylene MO, while the remaining π bond arises from the S_π MO of butadiene. We are concerned with the effect of the heteroatom on the course of this reorganization; thus, we consider the impact of the heteroatom on the π -MO's of the diene.

To this end, we can construct a diagram (Figure 2) representing the π MO's of butadiene and all the orbitals of the heterofragment X which are allowed by symmetry to interact with these π MO's. Oxygen has a $2p_\pi$ atomic orbital of species S, which may interact with the S_π MO of butadiene. This interaction, which would tend to stabilize the S_π MO, can persist through the reaction; however, as the S_π MO recedes to the interior of the butadiene fragment, the interaction would be weakened. The reactant would be stabilized relative to the products according to this argument; however, we have neglected the possibility of a stabilizing interaction of the S AO of oxygen with the S combination of the forming σ bonds. The two influences tend to cancel, leading us to expect that Diels-Alder addition to the furan molecule is possible under thermal conditions.

Determining the behavior of thiophene toward dienophiles is complicated by the possibility of d-orbital participation in the bonding. Sulfur has not only a

(7) Reference 2, p 65 ff.

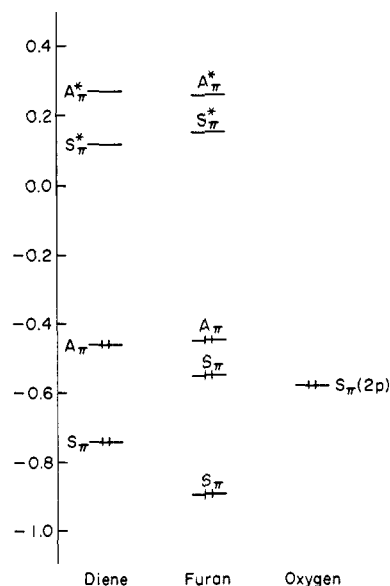


Figure 2. Orbitals of π symmetry for the diene fragment (left), an oxygen atom (right), and furan. The shifts in the A_π energy levels upon formation of furan are purely Coulombic effects.

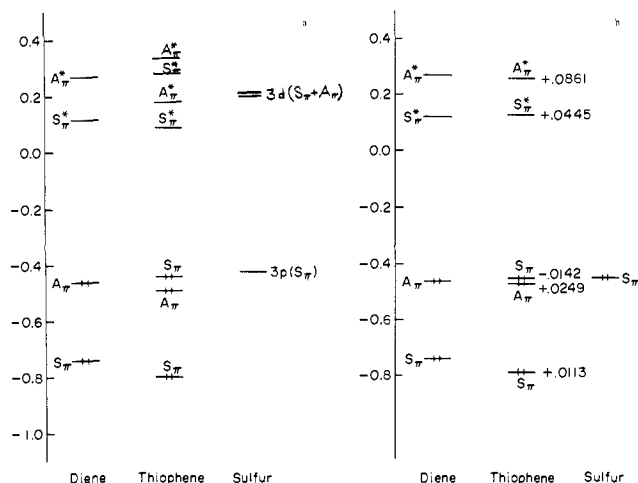


Figure 3. (a) Valence orbitals of π symmetry for the diene fragment (left), a sulfur atom (right), and thiophene. The 3d A_π level of sulfur stabilizes the A_π occupied MO of thiophene. (b) If the 3d levels of sulfur are not considered, the energy levels of thiophene shift as shown from the values computed with a full valence set of atomic orbitals.

3p atomic orbital of S_π symmetry but also a 3d orbital of that symmetry. Further, sulfur has a 3d orbital of A_π species, which may interact with the butadiene MO of A_π symmetry. It is necessary to estimate the effect of these 3d orbitals on the butadiene system and to judge how this effect changes during the course of the reaction. Accordingly, we have computed SCF MO's in the CNDO-2 approximation⁸ for thiophene and the ethylene adduct with two basis sets: the first allows only 3s and 3p orbitals to be occupied on the sulfur, while the second extends the basis set by placing the 3d orbitals on sulfur. Inspection of Figure 3 shows the impact of these d orbitals. It becomes apparent that the 3d orbitals have the most striking impact on the butadiene A_π MO. Whereas the A_π

(8) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N. Y., 1970.

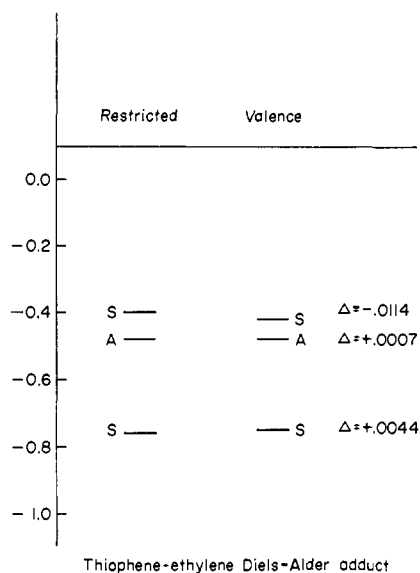


Figure 4. In contrast, the 3d levels of sulfur have very slight effect on the occupied MO energy levels in the Diels-Alder adduct of ethylene with thiophene. (These MO's are the correlates of those occupied MO's shown in Figure 3.)

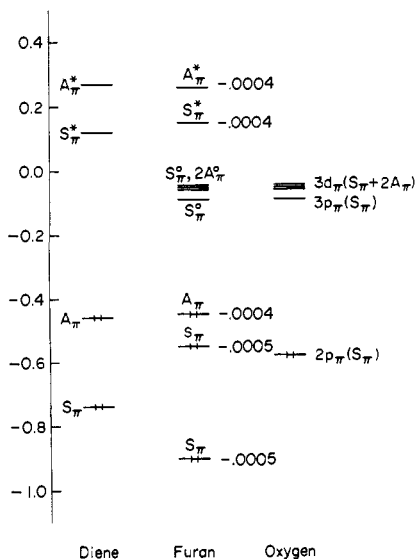


Figure 5. Incorporation of 3d and 3p AO's of π symmetry on oxygen shifts the energy of occupied MO's in furan only very slightly.

orbital is virtually unshifted in the reduced basis set from its energy in the isolated butadiene fragment, it is definitely stabilized by the 3d AO of A_π symmetry.

The question remains whether this stabilization of the A_π MO by the 3d level persists through the reaction. Figure 4 depicts the energy levels for the thiophene-ethylene adducts in the restricted (no d AO's) and valence (3s, sp, and 3d AO's on sulfur) basis sets. In contrast to the situation in the reactants, where the d orbitals had a net stabilizing effect on the orbitals in question, the d orbitals have little effect on the product MO's. In particular, the A_π MO, which was substantially stabilized in reactants by the 3d levels, is virtually unaffected in the products. We conclude that the Diels-Alder equilibrium would be forced toward the reactant's side insofar as the d orbitals of sulfur exert an influence. It is necessary to consider whether a

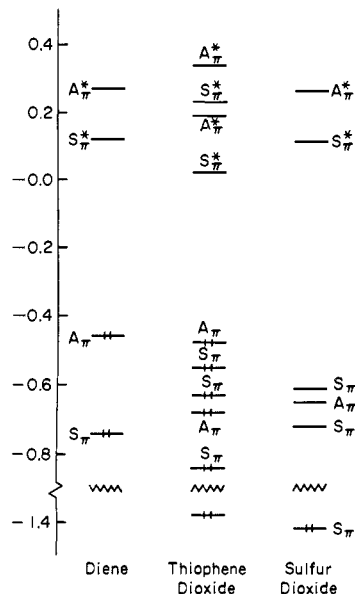


Figure 6. Valence MO's of π symmetry are shown for the diene fragment, SO_2 , and thiophene S,S -dioxide. The A_π MO arising predominantly from the diene enjoys a very slight stabilization.

picture similar to that described for the thiophene system would be obtained for furan if orbitals of d type were placed on the oxygen, and, if so, whether there is a difference in degree of the d orbital effect in thiophene from that in furan. In response to this question, we modified the CNDO program supplied by QCPE,⁹ to accommodate AO's of principle quantum numbers two and three on first-row atoms. Choice of CNDO parameters for the 3s, 3p, and 3d orbitals for oxygen was guided by the principle that it is valid to overestimate the effect of these AO's but not to underestimate their effect, since our object is to prove that d orbitals have little impact on the reactivity of furan. Thus the resonance parameter β was chosen to be the same for the $n = 2$ and $n = 3$ levels, even though the more diffuse orbitals would surely be less effective in bonding than the valence AO's. While the CNDO estimate of the diagonal elements of the core Hamiltonian matrix involves an average of ionization potential and electron affinity of some "average" valence state, it is difficult to define the electron affinity for the highly excited configurations involved here; still, it is almost certain that the electron affinities are small or negative. We would therefore overestimate the stability of the $n = 3$ levels by using the ionization potential only. Calculations on furan using the extended basis set and these "conservative" parameters lead to the orbital energies summarized in Figure 5. In brief, the d orbitals on oxygen are nearly inaccessible and have a negligible effect on the course of the Diels-Alder reaction.

Our final example is the condensation of thiophene S,S -dioxide. The SO_2 fragment provides three filled MO's of S_π symmetry and one filled MO of A_π symmetry, as well as a vacant orbital of S_π symmetry and a very remote vacant orbital of A_π species. The effect of the MO's on the butadiene fragment's levels is summarized in Figure 6. The highest occupied MO is of A_π species and is predominantly located on the

(9) Quantum Chemistry Program Exchange, Chemistry Department Indiana University, Bloomington, Ind. 47001.

butadiene; it enjoys a net stabilization due to the SO_2 , but the effect is not so pronounced as the stabilization in thiophene. This situation illustrates Pearson's rule that strong bonding requires strong overlap between an occupied MO of one species and an empty MO of the other species; when both levels are occupied, the system is not so strikingly stabilized by their interaction. In SO_2 the empty A_π MO is not so accessible either in overlap or on the energy scale as the empty A_π AO on sulfur. The reactant side of the equilibrium seems to be favored, since the A combination of σ bonds in the adduct is not much affected by the SO_2 fragment. The predictions that thiophene is substantially inhibited toward dienophiles, thiophene dioxide rather less aloof, and furan most hospitable of the three, are supported by the available experimental data.⁶

Mapping Study of Diels–Alder Condensations

The recently developed mapping analysis of concerted reactions¹⁰ is essentially an automation of considerations of charge reorganization in MO's in the course of reactions. The number called "state overlap" is zero for symmetry-forbidden reactions and increases as less charge reorganization becomes necessary in the reaction, reaching a maximum of unity for simple reorientations of the system. Application of the mapping analysis to the Diels–Alder reactions of interest here produced state overlaps of 0.32 for furan in its valence-shell basis, 0.32 for furan in the extended basis, 0.02 for thiophene in its valence basis, 0.30 for thiophene in its truncated basis (no d orbitals), and 0.20 for thiophene dioxide. Clearly, the state overlaps reflect the experimental behavior of these systems, and reliable predictions can be made without the laborious analysis of the previous section.

We do not propose that the mapping analysis can replace the perturbation-theoretic arguments, since the latter approach permits a satisfying "understanding" of bonding not supplied by mapping. However, the mapping analysis has several advantages in exploratory work which should be pointed out. First, since the mapping employs the MO wave function for the entirety of the reactant molecule(s) and product molecule(s), one is not likely to be misled by subtle participation in the reaction of substituents or neighbors which might seem inert. The effect of sulfur d orbitals in the Diels–Alder problem is a case in point. The elaborate consideration of d-orbital effects in the perturbation-theoretic study is automatically incorporated in the mapping analysis. Effects of neighbors on the course of a reaction have been discussed briefly elsewhere.¹⁰

The mapping analysis needs no symmetry. Any

(10) C. Trindle, *J. Amer. Chem. Soc.*, **92**, 3251, 3255 (1970); **91**, 4936 (1969).

system may be treated with ease, regardless of its symmetry or lack of it.

The mapping analysis is fast. This claim cannot be made for the original formulation,¹⁰ but mathematical refinements have been incorporated so that the mapping analysis of the thiophene dioxide–ethylene condensation required only 1.5 min on the Burroughs B5500 (comparable in speed to the IBM 360/40). The mathematical refinement lies in seeking the unitary transform T which obeys $T\phi_R = \phi_P$, where ϕ_R is the set of MO's occupied in the reactants and ϕ_P is the set of MO's occupied in the products. The equation quoted is not soluble exactly, but T can be defined so that the relationship is satisfied with minimum (least squares) error by a numerical method made available to us by Burton Garbow of the Argonne National Laboratory. The roots of the matrix T^+T are identical with the roots referred to in the original formulation of the mapping: that is, they are the squares of the overlaps of corresponding orbitals of reactants and products.

Finally, the mapping analysis can concentrate attention on the regions of a molecule critical to the allowed or forbidden nature of a reaction. In the Diels–Alder problem for thiophene, the orbitals associated with the smallest roots were localized in the C–S–C region. Inspection of these orbitals showed that the bonding to the A_π d orbital of sulfur in thiophene needed to be disrupted in order to obtain the condensed molecule. The insight provided by the mapping did in fact guide the development of the perturbation arguments presented above.

Note on Computations

The geometries for thiophene, furan, and ethylene were obtained from ref 11. The geometries for the bicyclic adducts were estimated by reference to the reported geometries of norbornane and norbornadiene, with appropriate small changes to accommodate average carbon–heteroatom bond lengths. The C–S–C bond angle in the thiabicyclic compounds was assigned the value 90° , which seemed to minimize ring strain. CNDO MO's were generated by a program distributed by the Quantum Chemistry Program Exchange, which we translated to Algol and adapted to the University of Virginia Burroughs B5500 installation. Modifications of this program to deal with extended bases on atoms in the series Li–F are described in a previous section of this report.

Acknowledgment. We are happy to acknowledge helpful conversations with Professor Richard Sundberg and Mr. Francis S. Collins.

(11) L. E. Sutton, Ed., *Chem. Soc., Spec. Publ.*, No. 11 (1958); No. 18 (1965).