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- (26) Following the completion of our work, we became aware that J. M. Lluch, Universidad Autonoma de Barcelona, had also solved kinetic Scheme I

exactly (unpublished work). We thank Professor E. L. Eliel for bringing this work to our attention and for helpful discussions.

- (27) **Note Added In Proof.** Following acceptance of this paper, N. S. Zefirov reported [*Tetrahedron*, **33**, 2719 (1977)] an analytical expression for A_4/A_1 for Scheme I at reaction completion. This expression does not include arbitrary initial conditions and does not describe the system as a function of time.

Secondary Orbital Interactions Determining Regioselectivity in the Diels–Alder Reaction. 3. Disubstituted Dienes

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Received October 17, 1977

Frontier molecular orbital theory is used to predict the regioselectivity in the Diels–Alder reactions of disubstituted butadienes. The primary orbital interactions which have been used by several investigators to predict the regioselectivity in the Diels–Alder reaction could not account for the regioselectivity observed with 1,2-disubstituted butadienes. When the secondary orbital interactions were included in the theory, the preferred regioisomer was predicted in every case. The frontier molecular orbitals of the dienes and dienophiles were determined by the CNDO/2, INDO, CNDO/S, and Hückel methods.

The regioselectivity of the Diels–Alder reaction has been successfully rationalized by considering only the interactions between the frontier molecular orbitals (FMO) of the diene and the dienophile.^{1–5} This approach is based on the second-order perturbation equation for the energy change which accompanies the orbital interactions of the two molecules involved in a cycloaddition reaction.⁶ From this theory several investigations^{2–5} have used the following generalizations to predict the regioselectivity: (1) the principle stabilization of the transition state arises from the HOMO–LUMO interaction which is the closest in energy (when the FMO interactions have similar energy separations, both interactions are considered); (2) the larger primary orbital coefficient of the diene will bond preferentially with the larger primary orbital coefficient of the dienophile. In fact, Anh et al.³ has recently applied this approach to approximately 100 examples of the Diels–Alder reaction.

In previous investigations we have found numerous cases in which this approach failed to predict the regioselectivity that was observed.¹ However, these discrepancies were eliminated when the secondary orbital interactions were considered. Consequently, we have added a third generalization in our approach which is as follows: (3) the secondary orbital coefficient of the dienophile will interact preferentially with the larger secondary orbital coefficient of the diene. By considering which regioisomers are favored by the interactions in generalizations 2 and 3 and the relative importance of these generalizations, the preferred regioisomer can be predicted.

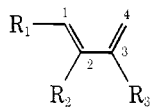
In this paper the above theories have been applied to the uncatalyzed Diels–Alder reactions of disubstituted butadienes. In these cases generalizations 2 and 3 favor different regioisomers and the experimentally preferred regioisomer varies with the substituent combination, thereby allowing a critical evaluation of the two theoretical approaches.

Results and Discussion

CNDO/2 calculations predict that the energy separation between the HOMO of the diene and the LUMO of the dienophile is considerably smaller than the energy separation between the LUMO of the diene and the HOMO of the dienophile for all reactions that have been investigated. Thus, the principle stabilization of the transition state will result from the former MO interaction and the latter can be neglected. Consequently, in the frontier molecular orbital approach the second-order perturbation equation simplifies into eq 1 and 2 for the two possible endo approaches of the dienophile to the diene.⁷ In the equations the γ_{cc} values are the atomic orbital transition state resonance integrals for the p_z carbon atomic orbitals. The c values are the atomic orbital coefficients in the respective molecular orbitals and the E values are the energies of the interacting frontier molecular orbitals.

Using CNDO/2 FMO energies and coefficients (Table I), the stabilization energy from the interaction of HOMO of the diene and the LUMO of the dienophile has been calculated for the various reactions. A resonance integral of 7 eV for the primary orbital interactions and a resonance integral of 2.8 eV for the secondary orbital interactions were used in the calculations. The value of 7 eV for the resonance integral of the primary orbital interactions was derived from the concerted transition state that ab initio calculations⁸ predicted for the cycloaddition of ethylene to butadiene along with consideration for the narrowing of the FMO energy separation in the transition state and a larger than experimental CNDO/2 energy separation between the interacting MO's. The resonance integral for the secondary orbital interactions was assigned a smaller value because the geometry of the transition state favors the overlap between the primary orbitals at the

Table I. Highest Occupied Molecular Orbitals of the Disubstituted Butadienes



R ₁	R ₂	R ₃	MO method	<i>P_z</i> coeff ^a				Energy of HOMO, eV
				C-1	C-2	C-3	C-4	
CH ₃	CH ₃ CONH	H	CNDO/2	0.578	0.357	0.180	0.336	-10.83
			INDO	0.577	0.340	0.169	0.317	-10.17
			CNDO/S	0.596	0.421	0.320	0.503	-8.65
			Hückel	0.622	0.421	0.238	0.466	
CH ₃	CH ₃ O	H	CNDO/2	0.580	0.410	0.225	0.402	-11.38
			INDO	0.585	0.393	0.210	0.380	-10.75
			CNDO/S	0.606	0.456	0.286	0.483	-8.80
			Hückel	0.627	0.434	0.258	0.490	
CH ₃	CH ₃	H	CNDO/2	0.561	0.456	0.284	0.468	-11.72
			INDO	0.562	0.453	0.296	0.475	-11.29
			CNDO/S	0.588	0.469	0.322	0.514	-8.89
			Hückel	0.592	0.444	0.316	0.546	
C ₆ H ₅ S	CH ₃ O	H	CNDO/2	0.296	0.300	0.094	0.231	-9.93
			Hückel	0.562	0.248	0.307	0.425	
CH ₃	C ₆ H ₅	H	CNDO/2	0.563	0.442	0.257	0.432	-11.64
			INDO	0.566	0.440	0.266	0.438	-11.15
			CNDO/S	0.596	0.469	0.311	0.499	-8.94
			Hückel	0.465	0.424	0.227	0.459	
C ₆ H ₅	C ₆ H ₅	H	CNDO/2	0.535	0.445	0.242	0.421	-11.46
			INDO	0.538	0.448	0.250	0.428	-10.92
			CNDO/S	0.589	0.475	0.303	0.495	-8.94
			Hückel	0.446	0.374	0.162	0.376	
H	CH ₃ O	C ₆ H ₅ S	CNDO/2	0.079	0.039	0.140	0.329	-10.50
H	Cl	CH ₃	Hückel	0.669	0.419	0.254	0.406	
			CNDO/2	0.519	0.322	0.319	0.497	-12.54
H	C ₆ H ₅	CH ₃	Hückel	0.579	0.364	0.378	0.602	
			CNDO/2	0.570	0.357	0.332	0.520	-12.15
H	C ₆ H ₅	CH ₃	Hückel	0.591	0.335	0.268	0.472	

^a These are absolute values. The other atomic orbital coefficients are zero for HOMO.

Table II. HOMO_{diene}-LUMO_{dienophile} Energy Difference between Regioisomers of the Disubstituted Butadienes

Diene	Registry no.	Dienophile	Registry no.	$\Delta E (E_{\text{meta}} - E_{\text{para}})$, kcal/mol ^{a,b}	
				Primary	Primary and secondary
1-Methyl-2-acetamido-1,3-butadiene	65442-04-8	Acrolein	107-02-8	6.710	2.182
1-Methyl-2-methoxy-1,3-butadiene	65415-12-5	Methyl acrylate	96-33-3	5.389	0.371
1,2-Dimethyl-1,3-butadiene	4549-74-0	Acrylonitrile	107-13-1	1.844	-1.694
1,2-Dimethyl-1,3-butadiene		Methyl acrylate		2.956	-2.026
1,2-Diphenyl-1,3-butadiene	5731-95-3	Acrylic acid	79-10-7	3.187	-2.536
1-Methyl-2-phenyl-1,3-butadiene	37580-41-9	Acrylic acid		3.764	-1.466
1-Phenylthio-2-methoxy-1,3-butadiene	65415-13-6	Methyl vinyl ketone	78-94-4	1.307	-2.197
2-Methoxy-3-phenylthio-1,3-butadiene	60603-16-9	Methyl vinyl ketone		-2.976	-1.951
2-Methoxy-3-phenylthio-1,3-butadiene		Acrylonitrile		-2.132	-1.336
2-Methyl-3-chloro-1,3-butadiene	1809-02-5	Acrylic acid		-0.733	-0.693
2-Methyl-3-phenyl-1,3-butadiene	18476-73-8	Acrylic acid		-1.527	-0.888

^a Meta or para to 2-substituent. ^b A negative energy difference favors the meta regioisomer while a positive energy difference favors the para regioisomer.

expense of the secondary orbital overlap.

From these stabilization energies the energy difference between the two possible regioisomers in the reactions of the 1,2-disubstituted butadienes was determined (Table II). In all of these reactions the primary orbital interactions favored the para (to the 2-substituent) regioisomer. However, the para regioisomer was preferred in only two of the analogous reactions that were found in the literature (Table III).⁹ If the secondary orbital interactions were included in the theory, the experimentally preferred regioisomer was predicted in every case.

Perturbation calculations were also carried out on the re-

actions of several 2,3-disubstituted butadienes (Table II). In these cases the calculations predicted that the primary interactions will dominate the secondary orbital interactions, in agreement with the experimental results.

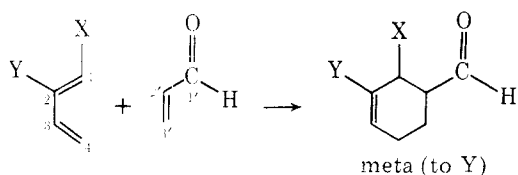
Furthermore, INDO and CNDO/S calculations were carried out on several of the dienes to determine the sensitivity of the coefficient magnitudes to changes in parameterization and the level of approximation. In every case the relative magnitudes of the HOMO coefficients from these SCF MO methods agreed with those of the CNDO/2 method (Table I).

The effect of the interaction between the HOMO of the dienophile and the LUMO of the diene on the theories' pre-

Table III. Preferred Regioisomer in the Diels–Alder Reactions of Disubstituted Butadienes

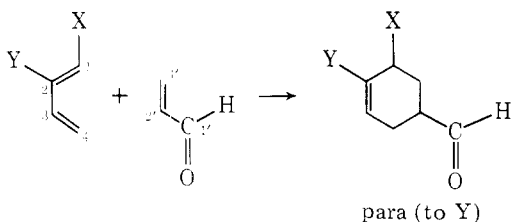
Diene	Dienophile	Preferred regioisomer	Ref
			<i>a</i>
			<i>b</i>
			<i>b</i>
			<i>b</i>
			<i>b</i>
			<i>b</i>
			<i>b</i>
			<i>c</i>
			<i>d</i>

^a L. E. Overman and L. A. Clizbe, *J. Am. Chem. Soc.*, **98**, 235 (1976). ^b Y. A. Titov, *Russ. Chem. Rev.*, **31**, 267 (1962). ^c B. M. Trost and A. J. Bridges, *J. Am. Chem. Soc.*, **98**, 5017 (1976). ^d T. Cohen, A. J. Mura, Jr., D. W. Shull, E. R. Fogel, R. J. Ruffner, and J. R. Falck, *J. Org. Chem.*, **41**, 3218 (1976).



$$E_{\text{meta}} = \frac{2(c_1c_2\gamma_{cc} + c_4c_3\gamma_{cc} + c_2c_1'\gamma'_{cc})^2}{(E_{\text{diene}}^{\text{HOMO}} - E_{\text{dienophile}}^{\text{LUMO}})} \quad (1)$$

primary interactions secondary interaction



$$E_{\text{para}} = \frac{2(c_1c_3\gamma_{cc} + c_4c_2\gamma_{cc} + c_3c_1'\gamma'_{cc})^2}{(E_{\text{diene}}^{\text{HOMO}} - E_{\text{dienophile}}^{\text{LUMO}})} \quad (2)$$

primary interactions secondary interaction

ditions was examined. No improvement in Anh's theory was found by including this MO interaction. Also, this MO inter-

action had no effect on the predictions from our approach. Furthermore, the π MO's lying below (subjacent) and above (superjacent) the FMO's were also considered. Though it is difficult to ascertain the importance of the interactions of these MO's in the transition state, no improvement in either theoretical approach could be found by the inclusion of these interactions. Furthermore, the molecular orbital methods did not agree on the actuality of the subjacent and superjacent molecular orbitals. In fact, the CNDO/S calculations which treat the β for σ and π overlap differently had no subjacent and superjacent π MO's which could affect the regioselectivity.

Anh et al.^{3,10} has indicated that simple Hückel calculations are superior to CNDO/2 calculations in the prediction of the preferred regioisomer in cycloaddition reactions. Consequently, Hückel calculations were carried out on the disubstituted dienes using Hess and Schaad's parameters¹¹ for sulfur and Streitwieser's parameters¹² which were found to give good predictions by Anh for all of the other atoms. The Hückel coefficients did not agree with the SCF MO coefficients in these cases (Table I), resulting in incorrect predictions in these cases. However, in defense of the Hückel method these cases contained sulfur or chlorine substituents for which the parameters may not be adequate.

Finally, the geometries used in the SCF MO calculations^{13,14} were determined by standard bond angles and bond lengths¹³ except for the sulfur–carbon bond and the $\angle\text{CSC}$ which were assigned values¹⁵ of 1.75 Å and 109°, respectively. Small changes in these bond angles and bond lengths did not affect

the interpretations. Also, the CNDO/2 method predicts that the preferred conformation of the phenyl group is perpendicular to the plane of the diene moiety for all dienes except 1-phenylthio-2-methoxy-1,3-butadiene. Consequently, this conformation of the phenyl group was used in those calculations.

Conclusion

The regioselectivity in the Diels–Alder reactions of disubstituted butadienes cannot be predicted from the primary orbital interactions. However, by including the secondary orbital interactions in the theory the preferred regioisomer can be predicted in all these cases.¹⁶ Furthermore, we have applied our approach to approximately 100 examples of the Diels–Alder reaction including 1-substituted, 2-substituted, 1,3-disubstituted, and 1,4-disubstituted butadienes as well as the reactions in this paper. In all these other cases, the preferred regioisomer was correctly predicted using CNDO/2 FMO energies and coefficients.

Acknowledgments. The authors thank the Virginia Commonwealth University Computer Center for a generous use of their IBM 370/158 computer. Also, T.C. wishes to thank the National Institutes of Health for partial support (GM-22760).

Registry No.—3-Acetamido-2-methyl-3-cyclohexene-1-carboxaldehyde, 65415-14-7; 4-acetamido-5-methyl-3-cyclohexene-1-carboxaldehyde, 65415-15-8; methyl 3-methoxy-2-methyl-3-cyclohexene-1-carboxylate, 65415-16-9; methyl 4-methoxy-5-methyl-3-cyclohexene-1-carboxylate, 65415-17-0; 2,3-dimethyl-3-cyclohexene-1-carbonitrile, 65415-18-1; 4,5-dimethyl-3-cyclohexene-1-carbonitrile, 65415-19-2; methyl 2,3-dimethyl-3-cyclohexene-1-carboxylate, 65415-20-5; methyl 4,5-dimethyl-3-cyclohexene-1-carboxylate, 65484-18-6; 2,3-diphenyl-3-cyclohexene-1-carboxylic acid, 65415-21-6; 4,5-diphenyl-3-cyclohexene-1-carboxylic acid, 65415-22-7; 3-phenyl-2-methyl-3-cyclohexene-1-carboxylic acid, 65415-23-8; 4-phenyl-5-methyl-3-cyclohexene-1-carboxylic acid, 65415-24-9; 2-methoxy-3-phenylthio-4-acetylcyclohexene, 65415-25-0; 1-methoxy-6-phenylthio-4-acetylcyclohexene, 65415-07-8; 1-methoxy-2-phenylthio-5-acetylcyclohexene, 60603-21-6; 1-methoxy-2-phenylthio-4-acetylcyclohexene, 60603-33-0; 3-methoxy-4-phenylthio-3-cyclohexene-1-carbonitrile, 60603-20-5; 4-methoxy-3-phenylthio-3-cyclohexene-1-carbonitrile, 65415-08-9; 3-methyl-4-chloro-3-cyclohexene-1-carboxylic acid, 35563-73-6; 4-methyl-3-chloro-3-cyclohexene-1-carboxylic acid, 65415-09-0; 3-methyl-4-phenyl-3-cyclohexene-1-carboxylic acid, 65415-10-3; 4-methyl-3-phenyl-3-cyclohexene-1-carboxylic acid, 65415-11-4.

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- (9) Some of the reactions were studied before the availability of modern separation techniques; consequently, the accuracy of the regioisomer ratios is not very great and the products which are formed by kinetic control have not been verified in these cases. However, more recent experimental data are available for the monosubstituted butadienes.⁹ By assuming that the substituent effects are additive, the preferred regioisomer can be predicted for the disubstituted butadienes from the regioisomer ratios of the monosubstituted butadienes. In every case the predicted and experimental regioisomers were the same.
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Observations Concerning the Scope and Mechanism of Photostimulated Reactions of Aryl Iodides with Diethyl Phosphite Ion. A Remarkable Difference in Behavior between *m*- and *p*-Chloriodobenzene¹

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Received August 16, 1977

Extending studies of the photostimulated reactions of diethyl phosphite ion with aryl halides to form diethyl arylphosphonates, we find that sodium and potassium diethyl phosphite serve equally well, that the reaction is suitable for use on a preparative scale, that the ortho, meta, and para isomers of the iodoanisoles and iodotoluenes all react satisfactorily, and that the iodobenzene/bromobenzene reactivity ratio is about 1×10^3 . In $S_{RN}1$ reactions of dihalobenzenes with nucleophiles, whether one or two halogen atoms are replaced depends on the nucleophiles and the halogens involved and on their orientation (meta or para in this study); reactions of the chloriodobenzenes are about the borderline between mono- and disubstitution.

Under photostimulation, aryl iodides react smoothly and quickly with diethyl phosphite ion to form diethyl arylphosphonate esters;^{3,4} see eq 1. The reaction occurs in a number of solvents, although ammonia or dimethyl sulfoxide is preferred. Observed quantum yields in Me_2SO greatly exceed unity;⁵ that and other facts indicate a chain mechanism, and the radical chain $S_{RN}1$ mechanism⁶ is believed to obtain.



The propagation cycle for the $S_{RN}1$ mechanism, which was first proposed (though without symbolization) by Kornblum⁷ and Russell⁸ and their associates for some substitutions at rather specialized aliphatic centers, is sketched in Scheme I.

Scheme I

