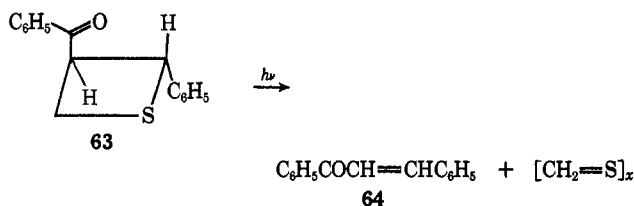*trans*-benzalacetophenone (64). The anticipated 2,3- and 2,4-diphenylthiophenes were not detected in the reaction mixture. This result indicates that the photo-

63

$$C_6H_5COCH\!=\!\!=\!CHC_6H_5 \quad + \quad [CH_2\!=\!\!=\!S]_x$$
64

chemistry of the thietane system proceeds by an entirely different path from that encountered in the azetidine series. The formation of *cis*- and *trans*-benzalacetophenone may be envisaged as proceeding by way of a homolytic cleavage of the benzylic carbon-sulfur bond. The resulting diradical undergoes subsequent fragmentation to thioformaldehyde and benz-

alacetophenone. The low bond dissociation energy of the C–S bond appears to be the major factor responsible for the difference in photochemistry of the two heterocyclic systems.

The foregoing examples have been considered in order to provide at least a partial indication of the intriguing and unusual transformations that small-ring ketones undergo upon electronic excitation. Considerable work in this area has been carried out by many investigators, and it may be safely anticipated that significant and new findings in small-ring photochemistry will be forthcoming in the future.

Recognition of Stereochemical Paths by Orbital Interaction

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The importance of orbital interactions, particularly between the HO (highest occupied) MO (molecular orbital) of one reactant and the LU (lowest unoccupied) MO of the other, in rationalizing chemical reactions is now invincibly evident.[2,3] Several papers have discussed this problem, giving a fair reasoning of the orbital interaction scheme.[4-6] The physical grounds for differentiation of the HOMO and LUMO from the other MO's have also been disclosed.[7]

The scheme of the HOMO–LUMO interaction between reacting species[2-4] has drawn the attention of organic chemists to the interpretation of the steric course of concerted processes, mainly through the elegant generalization of stereoselection rules and the classification of various stereospecific reactions by Woodward and Hoffmann.[5] Although a large part of their interpretation is based on the correlation diagram method, the orbital interaction scheme is also used in some parts, namely, in the explanation of the preferable paths of ring opening for cyclobutenes and for cyclopropyl derivatives, the dimerization of two ethylene molecules by an orthogonal approach, the migration of hydrogen or alkyl across a conjugated chain, the exo-endo selectivity in Diels–Alder-type cycloadditions, and the addition of ketenes to olefins. Obviously the correlation diagram criteria are not employed in some cases, such as interpretation of "sigmatropic" reactions, in which the reaction path has no usable symmetric character.

The purpose of this Account is to show that the HOMO–LUMO interaction scheme can in a unified manner be applied to various processes which have been mentioned and discussed by Woodward and Hoffmann,[5] and also to present, at the same time, an extremely simple and practical method to interpret or predict the favorable steric pathway. While this method is general in character, it is particularly suitable

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(2) For instance, see K. Fukui, "Molecular Orbitals in Chemistry, Physics, and Biology," P.-O. Löwdin and B. Pullman, Ed., Academic Press, New York, N. Y., 1964, p 513, and references cited therein, and subsequent papers on the frontier electron theory.

(3) (a) K. Fukui, *Bull. Chem. Soc. Jap.*, **39**, 498 (1966); (b) K. Fukui and H. Fujimoto, *ibid.*, **39**, 2116 (1966); (c) K. Fukui and H. Fujimoto, "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thyagarajan, Ed., Interscience, New York, N. Y., 1969, p 118; (d) K. Fukui, "Theory of Orientation and Stereoselection," Springer-Verlag, Heidelberg, 1970.

(4) (a) G. Klopman and R. F. Hudson, *Theor. Chim. Acta*, **8**, 165 (1967); (b) R. F. Hudson and G. Klopman, *Tetrahedron Lett.*, 1103 (1967); (c) G. Klopman, *J. Amer. Chem. Soc.*, **90**, 223 (1968); (d) L. Salem, *ibid.*, **90**, 543 (1968); (e) L. Salem, *ibid.*, **90**, 553 (1968); (f) L. Salem, *Chem. Brit.*, 449 (1969); (g) A. Devaquet and L. Salem, *J. Amer. Chem. Soc.*, **91**, 3793 (1969).

(5) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969); "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1969; and their preceding papers cited therein.

(6) R. G. Pearson, *Theor. Chim. Acta*, **16**, 107 (1970).

(7) (a) K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Jap.*, **41**, 1989 (1968); (b) K. Fukui and H. Fujimoto, *ibid.*, **42**, 3399 (1969).

for the interpretation of rather complicated reactions such as intramolecular rearrangements, to which the correlation diagram method is not always directly applicable. The theoretical basis is evident in light of previous papers.[2,3,7] This method is a practical representation of the fundamental proposition[3,4f,7b] that a *majority of chemical reactions should take place at the position and in the direction of maximum overlapping of the HOMO (or high-lying occupied MO's) and the LUMO (or low-lying unoccupied MO's) of the reacting species; in reacting species possessing a singly occupied (SO) MO, this plays the part of the HOMO or of the LUMO, or of both.*

Procedure

The process is illustrated in Figure 1 for the simple case of the thermal ring opening of cyclobutene. Usually chemical reactions occur in a certain limited region of the molecule.[3d,7b] The region essential to the conversion in this case is composed of one π bond and one σ bond to be broken and two π bonds to be formed. As a first approximation, it may be sufficient to take only these bonds into account. The reaction may be initiated by the mutual charge-transfer interaction between the π bond and the σ bond to be broken. The mode is illustrated in Figure 1. This interaction will take place between the HOMO and the LUMO of each bonding region. The HOMO is bonding and the LUMO is antibonding. The charge transfer to the antibonding LUMO from the bonding HOMO will cause the weakening, and accordingly the stretching, of both bonds. This principle is most easily understood if the diatomic case is thought of. An increase in bond length will cause a lowering of the LUMO level and an elevation of the HOMO energy, so that the charge transfer is further facilitated. Such interactions may be assisted by vibrational motion. As the reaction proceeds, the donor character of the C=C π bond and the acceptor character of the C—C σ bond become distinct, and the contribution of interaction I of Figure 1 becomes more important than that of I'.

The nodal properties of these MO's are characterized by the schematic diagram (Figure 1). The shaded and unshaded regions correspond to the plus and minus lobes of the MO's. Figure 1 indicates that the direction of effective overlapping of HOMO and LUMO in this case is that which is shown by arrows. It is concluded that the conrotatory change[5] would be favorable.

Here, a very elementary but important remark might be necessary. Each molecular orbital may have an indefiniteness by a factor of absolute value unity. Two different ways of shading are possible for each MO, if we are interested in real functions only. Physically, these ways represent an identical MO. Since the interaction energy between two systems, A and B, includes orbital overlapping between MO's belonging to A and B in the form of their absolute value or square,[2,3,7] the mode of change I* in Figure 2 can be expected with the same probability as that of I provided other conditions are the same. Note that these two modes of conrotatory
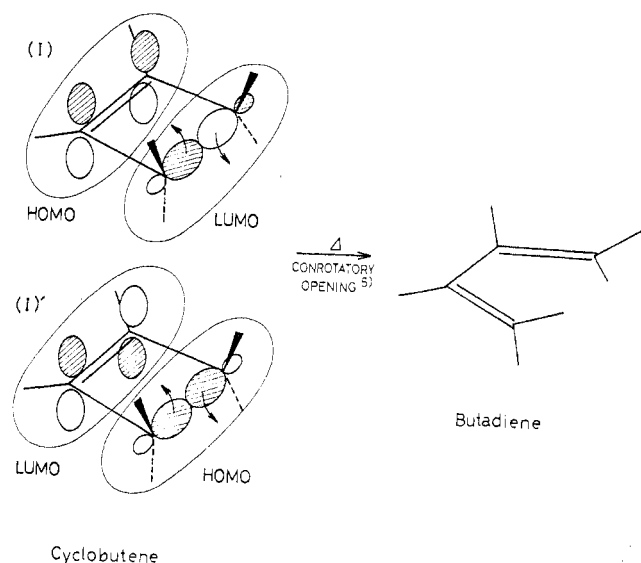

Figure 1. The mode of the HOMO–LUMO interaction in the ring-opening of cyclobutene.

change are not always equivalent if the molecule has appropriate substituents. Similar circumstances apply to the relation of II and II* of Figure 2. However, a useful convention may be adopted here in which we only refer to the "positive" overlapping such as I or II and do not care about the "negative" overlapping such as I* or II* for the purpose of using the maximum overlapping criteria. By this convention, the difference in the way of shading, as that between I and II, which is physically meaningless, turns out to distinguish two *different* modes of conversion. The two ways of shading the LUMO part in the models I and II are thus regarded as independent alternatives. In this way, we are able to consider hereafter only the direction which leads to shaded–shaded and unshaded–unshaded overlappings as the proper one which corresponds to bonding interaction, and at the same time we have to take *all* different ways of shading which may have the possibility of producing a nonequivalent direction. Consideration of Figure 4d and 4f will be helpful in understanding this relation.

In addition to this, a general remark is necessary concerning the choice of the region in the molecule in which we have to consider the HOMO–LUMO interaction. A fundamental guide may be: *the bordering surface of the two parts between which the HOMO–LUMO interaction is considered should be crossed by the newly formed bonds* (lemma A). This is required since the multicenter interaction between these two parts, taking place through the bonds to be formed, is the very origin of the stereoselectivity.

The practical value of such a convention will be clearer if we use a stereomodel like that shown in Figure 3. The HOMO and LUMO parts are specified with colored pegs. Two different colors are understood to represent the shaded and unshaded lobes of atomic orbitals (AO). For the sake of convenience, the σ bond to be broken has pegs just like those of sp[2] carbons and a
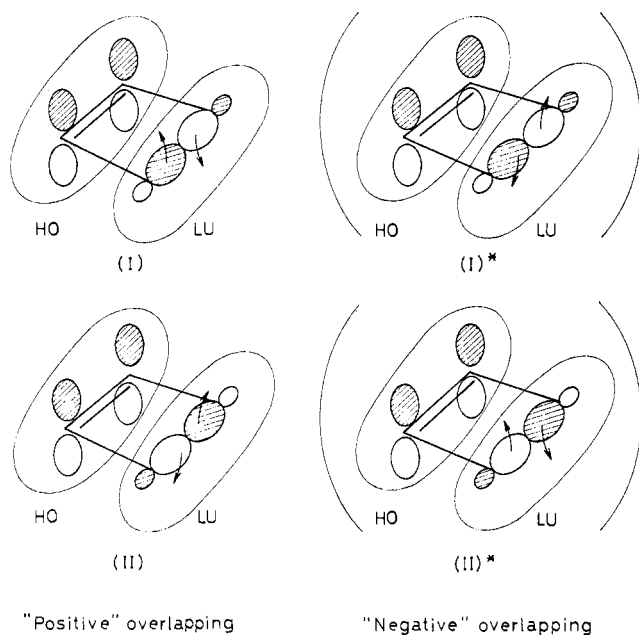
"Positive" overlapping   "Negative" overlapping

Figure 2. A convention used in shading MO's.
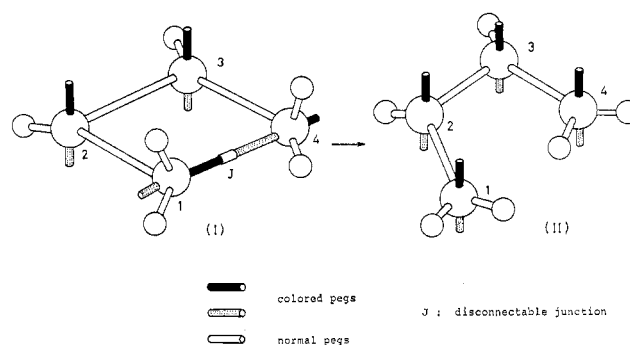
Figure 3. A stereomodel for the explanation by orbital interaction scheme.

disconnectable junction, J. The sp^3 "tail" pegs allow the model to represent the growth of the sp^3 hybrid to a p AO as the reaction proceeds. At first the colored pegs are properly placed so as to represent the nodal properties of the HOMO and LUMO. Then, junction J is removed and carbons 1 and 4 are rotated to form the 1,2 and 3,4 π bonds in such a way that two pegs of the same color become parallel on each side of a π bond that is forming. Of course, as mentioned before, the two nonequivalent ways of coloring lead to two nonequivalent pathways in the case of substituted cyclobutenes. We can simultaneously discuss the favorable or unfavorable steric circumstances with respect to these two paths by the use of such a stereomodel. It is known that the color relation of AO's between the two newly formed π bonds in the resultant molecule in Figure 3II is not physically significant since the color of the pegs only illustrates the direction of favorable change with respect to the partition of the molecule into the two parts illustrated in Figure 1I.

Examples

This simple method is powerful from the practical standpoint since it can reproduce the stereoselective reaction paths discussed in the comprehensive paper of Woodward and Hoffmann.[5] Several examples of intramolecular processes are given in Figure 4 (example o is discussed in ref 8) in which the sketch of a molecular model is replaced by the simpler representation as in Figure 1 for reasons of simplicity. If the reader experiments with a stereomodel, he will find it to be so simple and automatic that no explanation of the figure will be needed. In all of the examples mentioned, the two modes of HOMO–LUMO interactions like I and I' in

Figure 1 lead to the same conclusion. Therefore only the more important one of them is indicated in Figure 4. In excited-state reactions, too, only the SOMO–LUMO interaction is illustrated, since the SO'MO–HOMO interaction leads to the same conclusion. Symbols for the MO's used are defined in Figure 5. At the present stage of development we are forced to proceed with the assumption of reaction via the lowest excited state for these photoinduced processes. Literature references are completely omitted since the exemplification follows that of the Woodward–Hoffmann paper.[5]

Also, a few well-known examples of intermolecular processes are indicated in Figure 6 for comparison.[2,3] In addition, this method applies to stereoselective acyclic eliminations and additions.[3] The steric preferences of α,β-trans additions and eliminations, cis-α,γ-S_N2' reactions, α,δ-cis additions, and photoinduced α,β-cis additions are successfully explained.

In several examples of Figure 4, knowledge of a σ LUMO is needed. For such a purpose, the use of hybrid-based MO's[9] is recommended as most convenient. The nodal properties of σ MO's of conjugated molecules can be determined through such calculations.[9e]

Figures 4 and 6 exemplify two-center interactions, and Figure 7 gives examples of three-center reactions. These reactions, on the basis of the assumption of concertedness, can be treated as a combination of two two-center interactions in order to predict the direction of conversion in each bond fission or bond formation. Note that in each two-center interaction lemma A is obeyed.

Such a stepwise recognition of "concerted" reactions may at first sight seem to be self-contradictory, but it may rather be more reasonable than an attempt to understand every concerted multi-center reaction as a strictly "synchronous" change. Sometimes a bond fission may initiate the whole process, or it may happen that the conversion may start with a bond-forming

(8) (a) M. Jones, Jr., and L. T. Scott, J. Amer. Chem. Soc., **89,** 150 (1967). (b) The SOMO in Figure 4o is the same as the LUMO of the ground-state butadiene.

(9) (a) K. Fukui, "Modern Quantum Chemistry. Istanbul Lectures," Part I, O. Sinanoğlu, Ed., Academic Press, New York, N. Y., 1965, p 49, and references cited therein; (b) K. Fukui, "Sigma Molecular Orbital Theory," O. Sinanoğlu and K. B. Wiberg, Ed., The Yale University Press, New Haven, Conn., 1969, p 121, and references cited therein; (c) S. Katagiri and C. Sandorfy, Theor. Chim. Acta, **4,** 203 (1966); (d) J. A. Pople and D. P. Santry, Mol. Phys., **7,** 269; **8,** 1 (1964); (e) K. Fukui, H. Kato, T. Yonezawa, K. Morokuma, A. Imamura, and C. Nagata, Bull. Chem. Soc. Jap., **35,** 38 (1962).
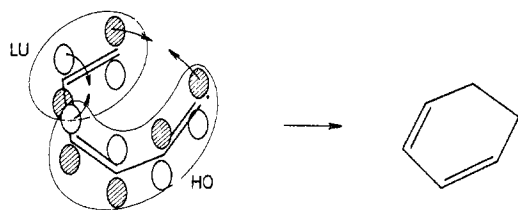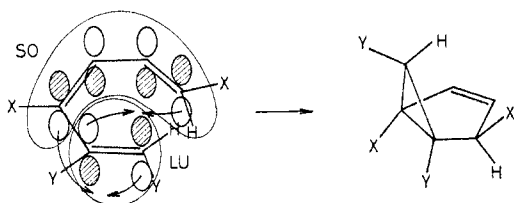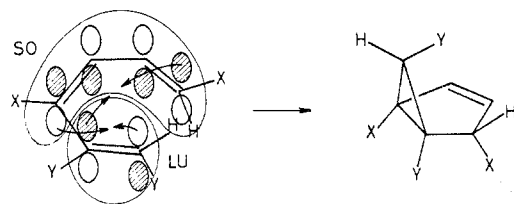
(a) Ring-closure of hexatriene (G).
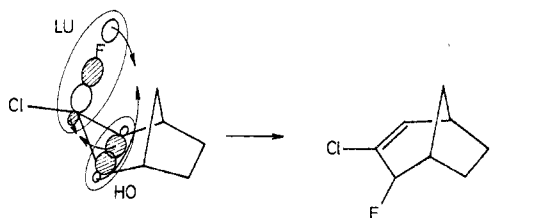
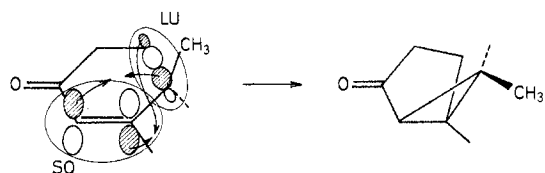(b) Selective rearrangement of 1,1-dihalocyclopropanes (G).
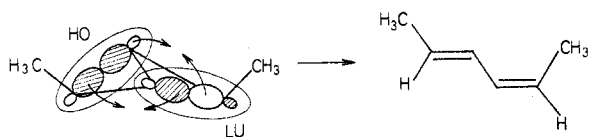
(c) Bicyclobutane rearrangement (G).

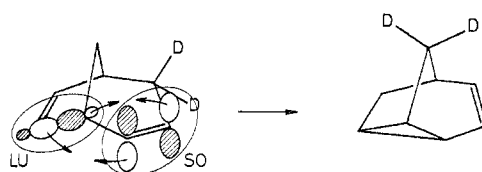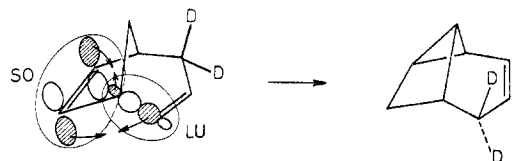(d) Bicyclization of hexatriene (E).

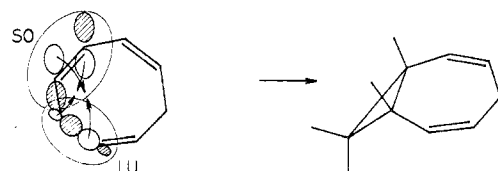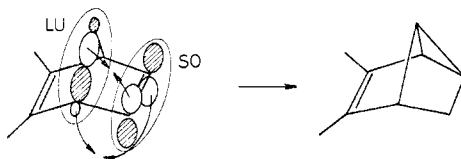(e) Cyclization of cyclohexenone (E).

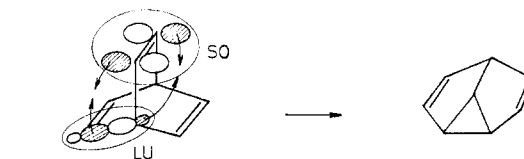(f) Bicyclooctadiene isomerization (E).

(g) Cyclization of cyclooctatriene (E).

(h) Cyclization of norbornadiene (E).

(i) Cyclization of bicyclooctatriene (E).

(j) 1,7-Hydrogen migration (E).

(k) Bicycloheptene rearrangement (G).

(1) Ring-opening of cyclopropyl cation (G).

(n) Fragmentation of five-membered diazene ring (G).

(m) Alkyl migration in bicyclohexenyl cation (G).

(o) Isomerization of bicyclo[4.2.2]-deca-2,4,7,9-tetraene
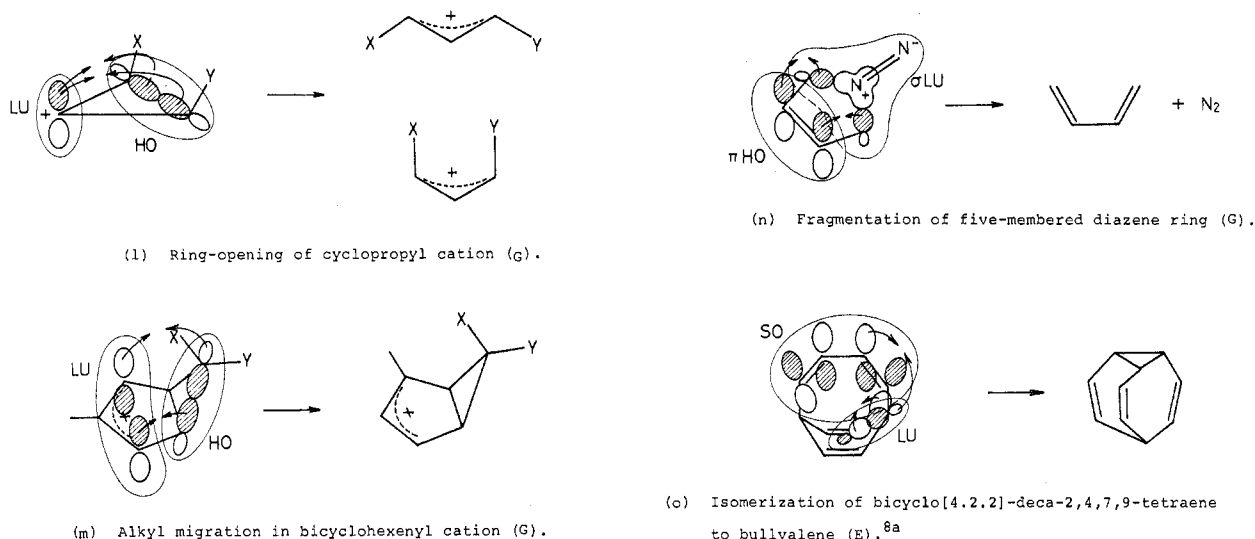to bullvalene (E).[8a]

Figure 4. Examples of orbital interaction involved in intramolecular stereospecific processes: (G) ground-state or thermal reaction; (E) excited-state or photoinduced reaction
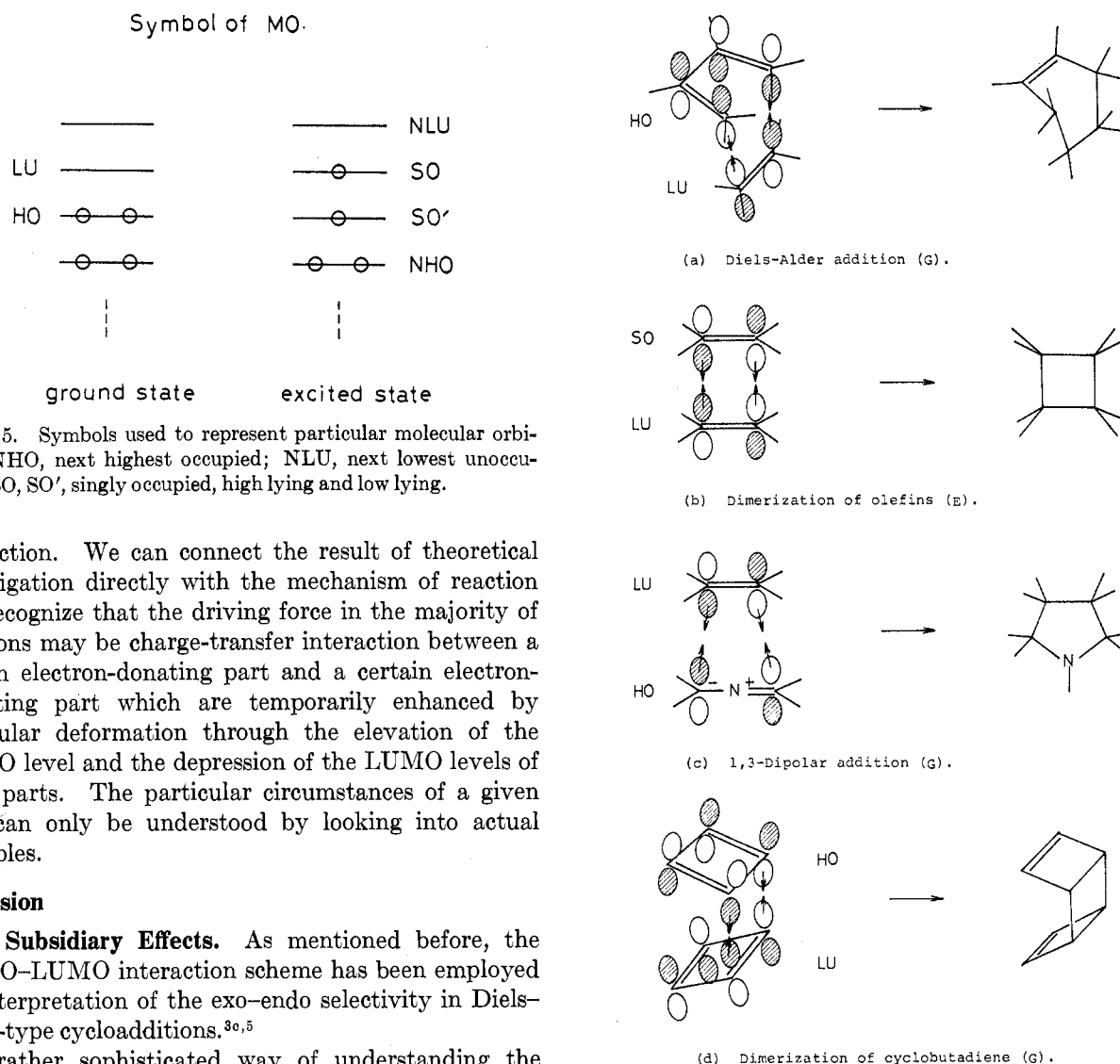
Symbol of MO.

NLU

LU   SO

HO   SO′

NHO

ground state   excited state

Figure 5. Symbols used to represent particular molecular orbitals: NHO, next highest occupied; NLU, next lowest unoccupied; SO, SO′, singly occupied, high lying and low lying.

(a) Diels-Alder addition (G).

(b) Dimerization of olefins (E).

(c) 1,3-Dipolar addition (G).

(d) Dimerization of cyclobutadiene (G).

Figure 6. Examples of intermolecular processes.

interaction. We can connect the result of theoretical investigation directly with the mechanism of reaction and recognize that the driving force in the majority of reactions may be charge-transfer interaction between a certain electron-donating part and a certain electron-accepting part which are temporarily enhanced by molecular deformation through the elevation of the HOMO level and the depression of the LUMO levels of these parts. The particular circumstances of a given case can only be understood by looking into actual examples.

Extension

(a) **Subsidiary Effects.** As mentioned before, the HOMO–LUMO interaction scheme has been employed for interpretation of the exo–endo selectivity in Diels–Alder-type cycloadditions.[3c,5]

A rather sophisticated way of understanding the boat–chair selectivity in the Cope rearrangement, which was adopted in the explanation given by Woodward and Hoffmann,[5] can be replaced by one based on the orbital interaction scheme. The nonbonding SOMO–

SOMO interaction has nothing to do with this selectivity since these MO's have a node at the central car-

(a) Cope rearrangement (G).

(b) Addition of olefin to norbornadiene (G).

(c) 1,4-Allyl migration (G).
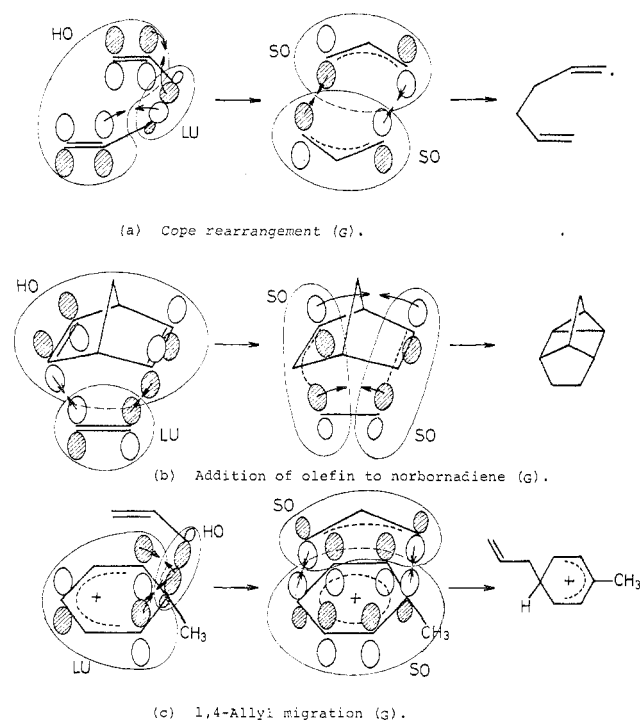
Figure 7. Examples of three-center reactions.

Chair   Boat

Figure 8. The boat–chair selectivity in the Cope rearrangement.

bon, as indicated in Figure 8. Consideration of NHO– and NLU–MO interactions leads to understanding the preference for chair-form transition states.

(b) Multiplicity Selectivity. The behavior of excited intermediates in the triplet state may be specified by their tendency to adopt a configuration in which two unpaired electrons are as far away as possible from each other, as is expected theoretically. For instance, cyclization in an excited triplet state can be specified by stating that cyclization usually takes place so as to pass through an intermediate which does not contain two unpaired electrons in one ring or in one conjugated chain, while an excited singlet-state reaction has no such restriction.[10] In this connection, the following lemma can be combined with the preceding method to predict the difference between triplet and singlet reactivities.[11-13] It is to be noted that concertedness is not necessarily expected in these cases. *In a triplet-state reaction each bond, which is to be newly formed through the overlapping of AO's of the two parts where the orbital interaction is considered, should be formed so as to result in a structure having two unpaired electrons not in conjugation with each other by virtue of that bond* (lemma B). Excited singlet-state reactions are not necessarily subject to such a limitation.

Figure 9 illustrates these circumstances. Figure 9A concerns the excited-state reaction of 1,3-pentadiene.[11,12] In the triplet-state reaction, the main product

is 1,3-dimethylcyclopropene, and 4-methylcyclobutene is not found. Diagrams ii-1 and ii-2 show that these processes do not meet the requirement of lemma B.

It is intersting to look into the reason why the biradical

is not formed in the process of i and ii-3. In this connection one should take into account the fact that the LUMO of propylene has a large extension at the carbon atom attached to methyl. An exaggerated sketch for
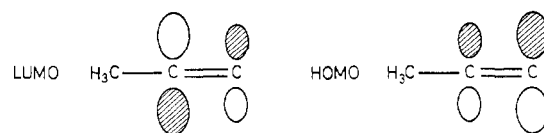
the mode of interaction may be

rather than

Figure 9B deals with the difference in reactivity in β,γ-unsaturated ketones. All examples[13,14] are considered to take place through the transfer of a n,π^* triplet to a π,π^* triplet. The examples of Figure 4e seem to belong to triplet-state reactions of the same category.[5] It has been established that the reaction of

(10) S. Kita and K. Fukui, *Bull. Chem. Soc. Jap.*, **42**, 66 (1969).

(11) (a) R. Srinivasan and S. Boué, *Tetrahedron Lett.*, 203 (1970); (b) R. Srinivasan, *J. Amer. Chem. Soc.*, **84**, 4141 (1962).

(12) S. Boué and R. Srinivasan, *ibid.*, **92**, 3226 (1970).

(13) (a) E. Baggiolini, K. Schaffner, and O. Jeger, *Chem. Commun.*, 1103 (1969); (b) J. Ipaktschi, *Tetrahedron Lett.*, 215 (1969); (c) W. G. Dauben, M. S. Kellogg, J. I. Seeman, and W. A. Spitzer, *J. Amer. Chem. Soc.*, **92**, 1786 (1970).
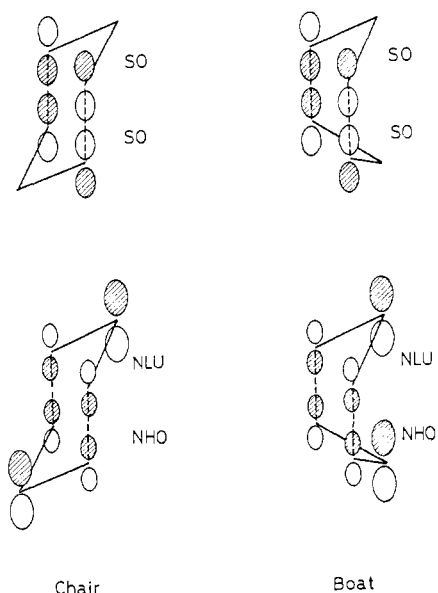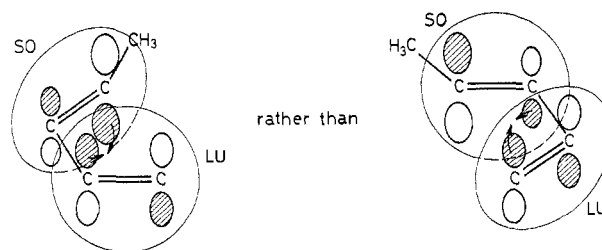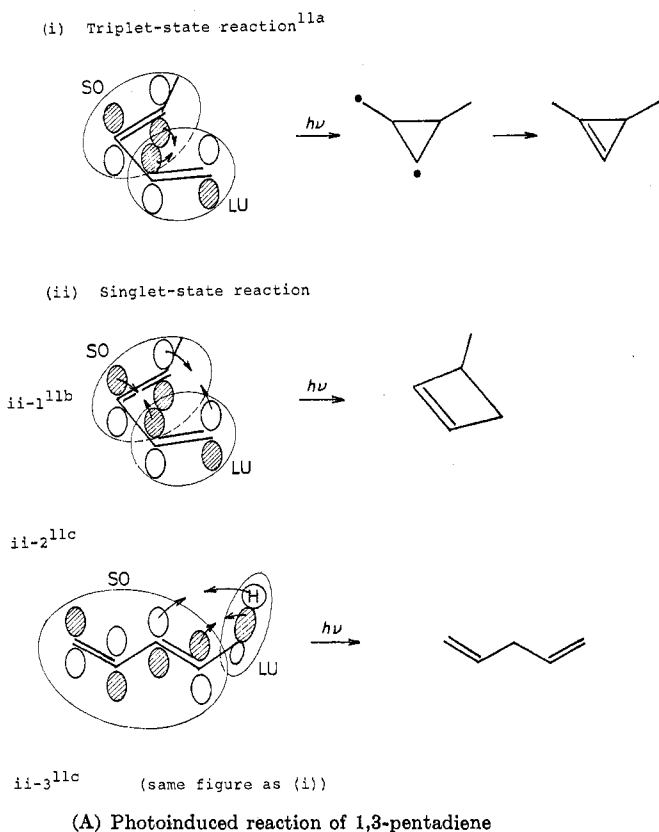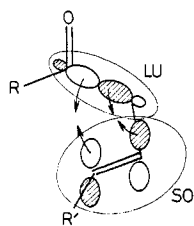
(i) Triplet-state reaction[11a]

(ii) Singlet-state reaction

ii-1[11b]

ii-2[11c]

ii-3[11c]   (same figure as (i))

(A) Photoinduced reaction of 1,3-pentadiene

(i) Singlet reaction

(ii) Triplet reaction

Examples of β,γ-unsaturated ketones:

(ref. 13a)   (ref. 13b)   (ref. 13c)
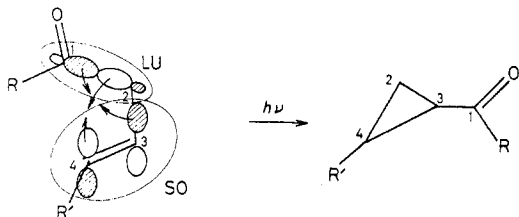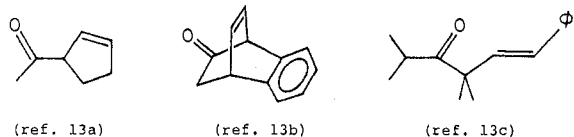
(B) Photoinduced reaction of β,γ-unsaturated ketones

Figure 9. The singlet–triplet selectivity.

a) Formation of benzvalene from benzene[16]

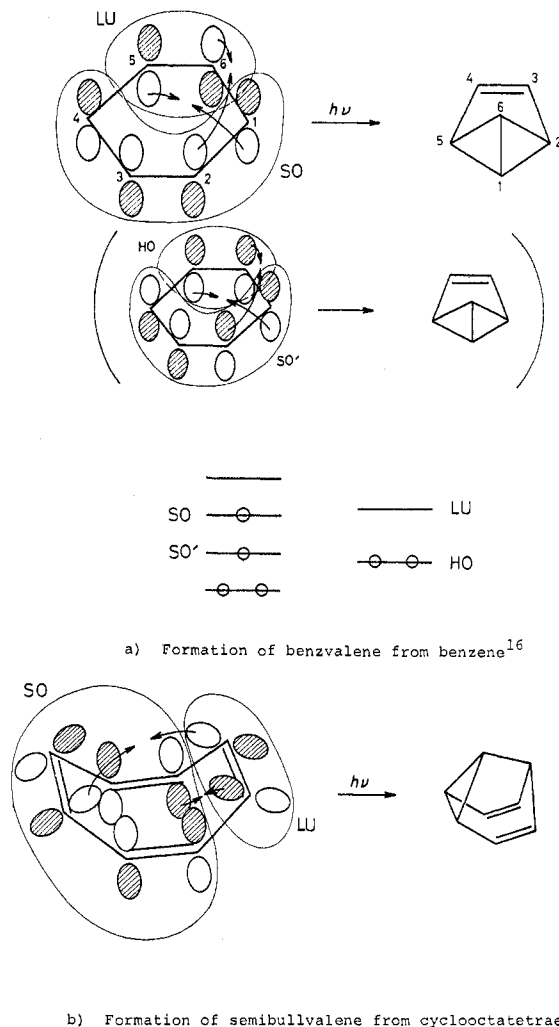b) Formation of semibullvalene from cyclooctatetraene.[17]

Figure 10. Examples of photoinduced multicyclization.

ucts in complicated photochemical multicyclization processes of unsaturated systems. Although it may not be possible to establish concertedness, this is never an essential point in the present discussion. Examples of some multicyclization processes are illustrated in Figure 10.

Merits

The HOMO–LUMO interaction scheme, in combination with a numerical calculation, is obviously applicable to any system with ambiguous symmetry properties. It may happen that the conjugative influence of neighboring parts exerts an influence on the orbital extension and on the nodal properties of the HOMO or LUMO, and, clearly, this method applies even in such cases and can give information on these effects.

Orbital symmetry is a most important factor in determining the magnitude of delocalization stabilization due to the HOMO–LUMO overlapping.[2,3] However, it

Figure 4i proceeds through a triplet state.[15] All of these cases satisfy the requirement of lemma B.

(c) **Multicyclization.** A useful extension of these ideas might be the prediction of the structure of prod-

(15) H. E. Zimmerman, R. W. Binkley, R. S. Givens, G. L. Grunewald, and M. A. Sherwin, *J. Amer. Chem. Soc.*, **91**, 3316 (1969).

(16) K. E. Wilzbach, J. S. Ritscher, and L. Kaplan, *ibid.*, **89**, 1031 (1967).

(17) H. E. Zimmerman and H. Iwamura, *ibid.*, **90**, 4763 (1968).
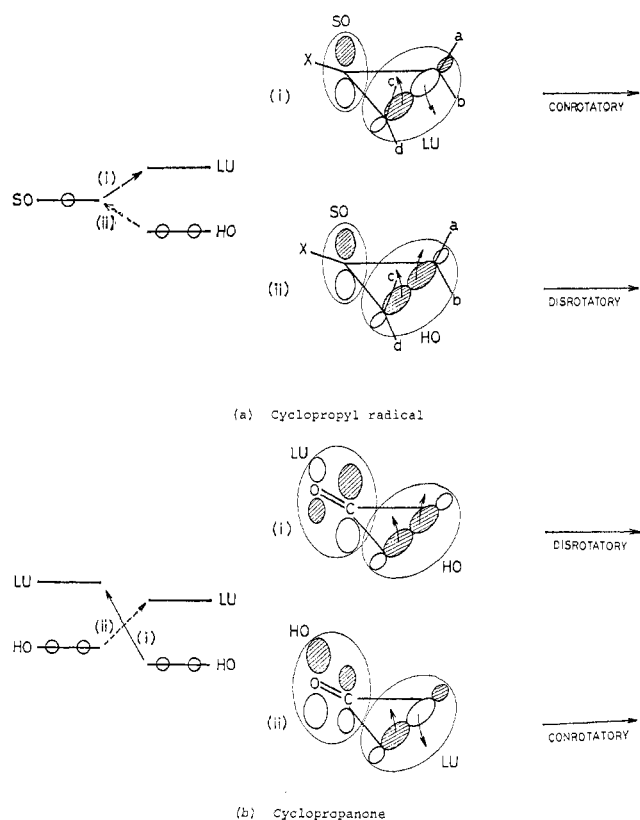
(a) Cyclopropyl radical

(b) Cyclopropanone

Figure 11. Continuity in the stereoselection in thermal ring-opening reactions.

should be noted that the existence of symmetry elements in orbitals is *not* essential in the recognition of favorable reaction paths. This point should be obvious from the previous discussion.

The examples shown in Figure 11 illustrate that stereospecificity is predicted to be continuous, provided that the related factors are continuous. In the ring-opening reactions of cyclopropyl radical (a), the results of prediction by a LUMO-SOMO interaction (i) and HOMO-SOMO interaction (ii) are opposite. The favorable path may be subject to substituent effects as well as electrocyclic control. Elevation of the SOMO energy will make the LUMO-SOMO interaction dominant, and lowering of the SOMO level may increase the importance of HOMO-SOMO interaction. In this way, the direction of change may vary.[18] A similar situation is expected in the ring opening of cyclopropanone (b). However, in view of the large amplitude of the LUMO at the carbonyl carbon in this instance, case i is expected to prevail.[19]

As one of the merits of the present method, it may be

pointed out that the orbital interaction scheme can always give the directional features of the reaction mechanism at the point of initiation and the force which acts along the reaction path and thus drives the system to further conversion. In this connection, the use of stereomodels will facilitate the discarding of difficultly accessible steric paths when it is combined with consideration of *positive* overlap of the particular orbitals previously mentioned.

An interesting application of this method is the explanation of the catalytic action of d-orbital participation which causes an otherwise "symmetry-forbidden" reaction to become "allowed."[3d] Applications are also possible to the prediction of molecular stability and the stability of configurations of molecular species[3d] and to explanations of "spiroconjugation"[20] and "bicycloaromaticity."[21]

This method requires no selection rule and is completely automatic. Usually, only knowledge of the HOMO and LUMO of very simple systems is needed, and this makes the theory quite simple and extendable and gives it a uniform character.

Of course, reactivity in all types of unicentric reactions of saturated and unsaturated compounds can be interpreted by the HOMO–LUMO interaction method.[2,3] Problems of orientation and stereoselection can thus be discussed in a unified fashion by this approach.

So far, few contradictions have been found between predictions based on the correlation diagram method and the orbital interaction criteria, but the latter are able to treat many problems which are beyond the reach of the former method.

The understanding of complicated stereospecific organic reactions and the generalization of stereoselection rules made by Woodward and Hoffmann are unquestionably valuable. A relevant way of reasoning to a result should lead to an understanding of the underlying nature of chemical reactions. The correlation diagram method based on the principle of conservation of orbital symmetry is one way of reasoning; however, the orbital interaction scheme appears to be more unificative and wider in scope, and it gives more direct descriptions of the nature of chemical reactions.

(18) *Cf.* H. C. Longuet-Higgins and E. W. Abrahamson, *J. Amer. Chem. Soc.*, 87, 2045 (1965).

(19) *Cf.* the prediction made by N. J. Turro, *Accounts Chem. Res.*, 2, 25 (1969).

(20) H. E. Simmons and T. Fukunaga, *J. Amer. Chem. Soc.*, 89, 5208 (1967).

(21) M. J. Goldstein, *ibid.*, 89, 6357 (1967).