

TOPOLOGY OF CHEMICAL REACTIONS .III.<sup>1</sup> DIELS-ALDER REACTION

R.S.Lall

Department of Chemistry  
St. Andrew's College,  
Gorakhpur 273001, U.P., India.

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ABSTRACT

A topological representation of the Diels-Alder reaction is reported. In non-symmetrical systems, the chances of two bonds formation or breaking differ. The algebraic demonstration, thus, shows that a two-step mechanism is more favourable in non-symmetrical systems.

INTRODUCTION

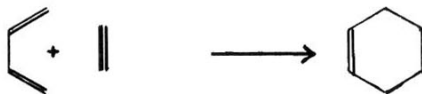
In recent years the use of graph theory<sup>2,3</sup> is becoming popular for studying various problems in chemistry<sup>4-9</sup>. In chemistry the term molecular topology is generally used to represent molecular graphs. In molecular graphs the atoms are represented by vertices and the chemical bonds by edges. These graphs are used to construct a number of matrices associated with them<sup>2</sup>. Several authors<sup>4-9</sup> have used these matrices to construct topological indices to characterise the molecular systems in terms of physical and chemical behaviour and to calculate molecular orbital energies, in the frame-work of Hückel Molecular Orbital theory<sup>10</sup>. Chemical graphs in different sense

are used by others<sup>11-15</sup> to explain the reaction mechanism or the nature of transition states in various organic reactions. More recently, Sinanoğlu<sup>16-17</sup> discussed the topology of chemical reaction networks in terms of all possible reaction mechanisms or pathways as a function of the number of reaction steps or species.

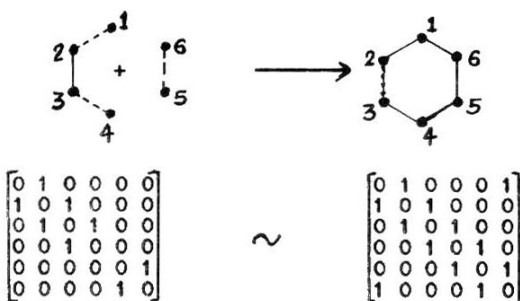
In our previous work<sup>1,18</sup> we have developed a topological representation of bond breaking and bond formation in the chemical reactions involving carbon skeletons, in which the elementary transformation operations were applied to the adjacency matrix of the reactant graph. In the present investigation we have discussed the Diels-Alder and the retro-Diels-Alder reactions<sup>19-20</sup>. Diels-Alder reactions are important in organic syntheses as they involve an addition of two carbon skeletons to produce a six membered ring in all cases<sup>21</sup>. Results of the topological methods are in agreement with the observed experimental facts and also some new results are obtained with respect to the regioselectivity in Diels-Alder reactions of the non-symmetrical dienes and dienophiles. Ugi<sup>22</sup> has also discussed the similar idea based on the bond and electron (BE) matrices. Whereas in the present communication we have discussed the problem in the light of adjacency matrices.

#### MATRIX COMPUTATION

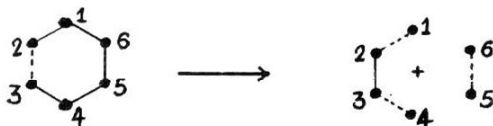
Diels-Alder reactions are (4+2)-cycloaddition<sup>23</sup> reactions in which a double bond adds 1,4 to a conjugated diene, so that the product is always a six-membered ring. The double bond compound is called a dienophile. A general reaction is



The topological representation<sup>18</sup> of this process is,



The double bonds are represented by dotted lines in the graph. The retro-Diels-Alder reaction of cyclohexene is represented in the same manner,

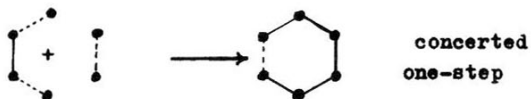


The elementary rows/columns transformation operations applied to the adjacency matrix are, thus, shown to represent a general bond formation/ bond breaking process.

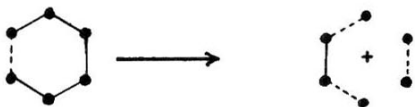
### REACTION MECHANISM

There are two possible mechanisms for the Diels-Alder reaction which have been considered<sup>23</sup> 1) Concerted, pericyclic, involving a cyclic six-membered transition state and no intermediate, and ii) a two step pathway with a diradical intermediate. The topological method predicts both of these mechanisms. But a two step mechanism is more favourable for the reactions involving non-symmetrical dienes and dienophiles. The concerted one step pathway is predicted by the equal chances of bond formation and bond breaking in the Diels-Alder and retro-Diels-Alder reaction in symmetrical systems, in terms of

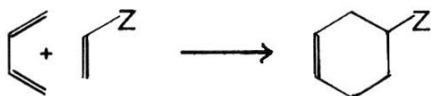
equal chances of rows/ columns transformation,



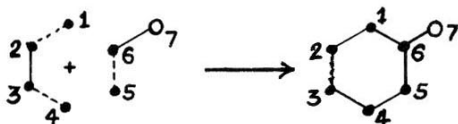
In retro-Diels-Alder reaction , the graphs are shown as,



In non-symmetrical systems, the reaction may be represented in general,



The graphical representation of the process is,



The vertex (O) is a side group. The matrix transformation is represented by an overall transformation,

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix} \sim \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$$

The formation of bond 1,6 is followed by a transformation  $R_1 + R_7 / C_1 + C_7$  i.e. row 7 is added to row 1 and column 7 is added

to column 1. But if we proceed to make the bond 4,5 first , we have to follow the operation  $C_5 + (C_3 - C_1)$  and  $R_5 + (R_3 - R_1)$  , i.e. row 5 is added to row 3 minus row 1. This operation is one step longer than the operation performed to make the bond 1,6 . This shows that the formation of 1,6 bond is easy and in the actual mechanism it may form first. Thus the chances of formation for the two bonds differ and the reaction will proceed through a two step pathway.

The retro-Diels-Alder reaction of a non-symmetrical system is represented by,



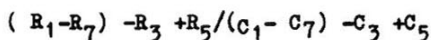
The topology of the process is represented by seven vertex graphs. In matrix transformation, to break the bond 1,6 first one should operate as,

$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix} \xrightarrow{R_1 - R_7 / C_1 - C_7} \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$$

and then to break the bond 4,5 , the operations should be,

$$\underline{R_1 - R_3 + R_5 / C_1 - C_3 + C_5} \quad \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$$

to get the final result. But if one breaks the bond 4,5 first he has to perform the operations,



to get the desired result. This process includes the operation  $R_1-R_7$  i.e. the breaking of the bond 1,6. Hence, it is concluded that the chances of breaking of the bonds 1,6 and 4,5 differ and it is easier to break the bond 1,6 first than bond 4,5. This simply means that the vertex of higher degree provides more chances of rows/ columns transformation in the adjacency matrix. To explain the reaction mechanism, we can say that the reaction proceeds through a two step pathway and is not a concerted one. In general, for non-symmetrical systems the Diels-Alder and the retro-Diels-Alder reactions could proceed through a two step pathway. Two step mechanism is recently discussed by Dewar<sup>24,25</sup>

#### NATURE OF THE DIENOPHILE

It is known<sup>23</sup> that the reaction is easy and rapid when the dienophiles are of the form,

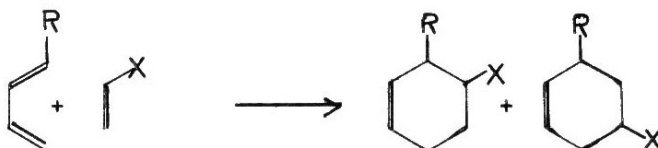


where Z and Z' are CHO, COOH, COR, COOR, COCl etc. The topological results are in agreement with these observed facts. The presence of a side group or substituent provides more chances of rows/columns transformations. This is explained above by taking seven vertex graphs. The process may be extended to represent a number of other similar reactions, for example the reaction of two dienes<sup>26</sup> and the reaction of butadiene and isoprene.<sup>27</sup> The structures generated by matrix transformations show a clear agreement with the possible adducts obtained in these reactions.

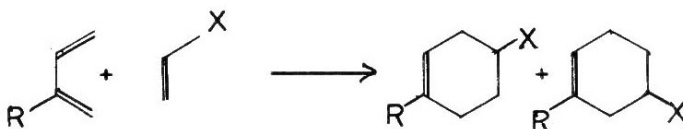
#### STEREOCHEMISTRY AND REGIOCHEMISTRY

The stereochemistry of the Diels-Alder reactions is explained in terms of the nature of the products and their

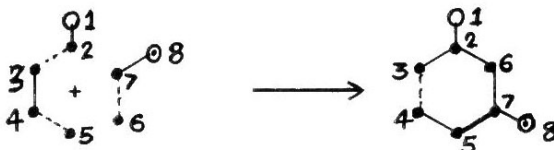
representative graphs. The regioselectivity can be discussed by matrix transformation method. The formation of isomeric adducts from non-symmetrical dienes and dienophiles, is shown as,



and



In these reactions mixtures of products are obtained. Usually the 'ortho' and 'para' products are favoured<sup>28</sup>. This regioselectivity is explained by molecular orbital methods<sup>29</sup>. Experiments show that, the 'ortho' and 'para' products are more stable<sup>30</sup>. Molecular orbital calculations<sup>29</sup> predict that 'meta' products should predominate over the 'ortho' or 'para'. Topological calculations based on the matrix transformation are in agreement with the theory<sup>29</sup>. For example, in the following reaction,



$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix} \sim \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$$

The operations  $R_1+R_6$  and  $C_1+C_6$  and  $R_8+R_5$  /  $C_8+C_5$  leads to the formation of bonds 2,6 and 5,7, while no direct operation leads to the formation of bonds 2,7 and 5,6. Thus, the matrix manipulation yields 'meta' isomer and not the 'ortho'.

## DISCUSSION

The detailed mechanism of the Diels-Alder reaction is still unknown. Whether the reaction is one-step concerted or two-step biradical process, is a matter of discussion. The course of a chemical reaction cannot be followed directly by any known experimental technique. Therefore the theoretical calculations can give an idea about the reaction mechanism. In recent years, various attempts have been made from time to time to study the Diels-Alder reaction theoretically, e.g., CNDO<sup>31</sup> or computer-assisted Roothan-Hall<sup>32</sup> calculations and semiempirical procedures (MINDO/2 and MINDO/3)<sup>33</sup>. McIver and Komornich<sup>34</sup> applied MINDO/2 procedure and Dewar<sup>24,33</sup> applied MINDO/3 procedures. Dewar<sup>24,25</sup> has shown that the transition state is very unsymmetric, one of the new CC bonds being formed first. In 1978, Dewar<sup>25</sup> published the same unsymmetrical nature of the transition state in retro-Diels-Alder reaction.

The topological results in this investigation provide an idea about the reaction mechanism. In non-symmetrical systems, the mechanism is explained in terms of the chances of bond formation or bond breaking, considering the



seven vertex graphs. In matrix transformation method, we have seen<sup>18</sup> that a vertex of higher degree provides more chances of rows/columns transformations. This shows that it is easy to form or break the bond which is nearer to the substituent, as in the case of substituted dienes or dienophiles. The reaction in non-symmetrical systems thus, proceeds through a non-concerted two step path, i.e., one of the two CC bonds should break first, supporting Dewar's<sup>24,25</sup> work.

The structure-activity relationships and the nature of the dienophile show that the reaction is activated by substituents irrespective whether it is electron withdrawing in some cases or electron donating in other cases. The topology of the reaction is in favour with the observed facts<sup>23</sup>. The method can also be extended to similar reactions involving heterocyclic compounds.<sup>35</sup>

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