Simple Prediction of Regiospecificity in Diels–Alder Reactions

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Summary Application of the "hard and soft" concept to the Woodward–Katz model allows simple and accurate prediction of the structure of the major product in Diels–Alder reactions.

DIELS–ALDER reactions between two dissymmetrical reagents are most likely non-synchronous, as suggested by Woodward and Katz.[1] If now one can predict which σ bond has the greatest probability of being formed first, the problem of the regiospecificity of the reaction is solved at the same time. As Diels–Alder reactions have been shown to be under frontier control,[2] it seems reasonable to think that the first bond would link the softest[3] centres, *i.e.* atom C_i of the first molecule and atom C'_j of the second molecule such that:

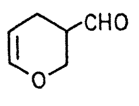
$$\sum_{m}^{\text{occ}}\sum_{n}^{\text{unocc}}\frac{(a_{im}\,a'_{jn})^2}{E'_n-E_m}+\sum_{m}^{\text{unocc}}\sum_{n}^{\text{occ}}\frac{(a_{im}\,a'_{jn})^2}{E_m-E'_n}$$

has the greatest value. In this expression, a_{im} is the coefficient of C_i in the mth M.O., a'_{jn} the coefficient of C'_j in the nth M.O. and E_k the energy of the kth M.O.

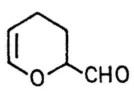
It is generally sufficient to consider the frontier orbitals. The rule is even simpler for reactions between two different compounds, where one molecule has usually a highest occupied M.O. (H.O.) and the other a lowest vacant M.O. (L.V.) very near the nonbonding level. The softest centre of the first (second) molecule is then the atom having the greatest coefficient in the H.O. (L.V.)

The foregoing rule has been tested on about a hundred examples, using simple Hückel calculations with Herndon's parameters [4] For 30 reactions chosen at random, we also used two other sets of parameters suggested respectively by Streitwieser[5] and by Julg and Julg.[6] The conclusions are always the same.

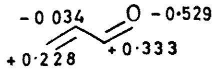
The chart shows some of the reactions investigated. Every time, our rule predicts correctly the structure of the major product. An interesting case is the dimerization of acraldehyde which can give (1) or (2) (the only observed product). Huckel orbital interactions predict both products.[2b,7a] SCF calculations give the correct orientation. The major contribution to the stabilization of (2) relative to (1) arises then from the electrostatic terms.[7b] This is somewhat confusing as considerations of net charge densities in acraldehyde (3) would lead to the wrong prediction.[1] Application of the present hypothesis (orbital interactions of the terminal carbon atoms only) predicts the correct product.



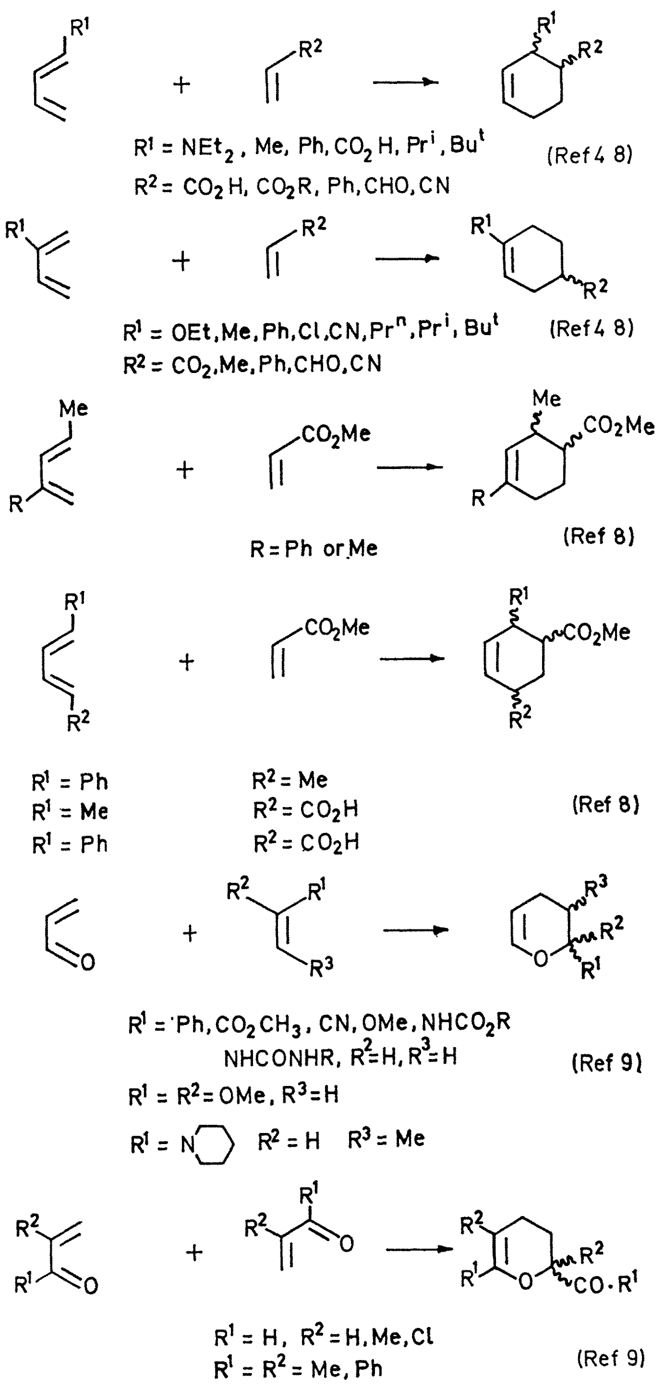
(1)



(2)



(3)



CHART

Application of the same rule to 1,3 dipolar and 2 + 2 cyclo-additions is under study in our laboratory.

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