Tetrahedron Letters No. 10, pp 915 - 918.
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0040-4039/79/0301-0915$02.00/0

SUBSTITUENT EFFECTS OF SIGMATROPIC REARRANGEMENTS AND CYCLOADDITIONS[1]

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Sigmatropic rearrangements and cycloadditions are subject to strong rate-enhancing substituent effects. For cycloadditions, such effects are usually interpreted in terms of transition state stabilization as estimated by 2nd order perturbation theory.[2] Recently, Hückel calculations have been used in an effort to reach a qualitative explanation for the influence of substituents on pericyclic reactivity.[3]

Here, the activation energies for the norbornadiene-cycloheptatriene rearrangement, the Cope rearrangement and the Diels-Alder reaction are shown to correlate linearly as $\Delta E^{*} = \alpha \cdot \Delta\varepsilon$, where α is an empirical constant characteristic of the reaction and $\Delta\varepsilon$ is the calculated energy difference between the active orbitals,[4] _i.e._ the filled bonding orbital and the empty antibonding orbital describing the bonds that are formed and broken in the reaction.

Detailed studies of interactions between filled and empty orbitals in chemical reactions are not possible using common methods for MO-calculations, the virtual orbital energies of which do not correspond to those of the excited orbitals. HAM/3, however, a newly developed semi-empirical method, correctly predicts photo-electron and uv-spectra of organic compounds.[5] Moreover, the eigenvalues of the molecular orbitals computed by this method are defined as the partial derivative of the total electronic energy with respect to the occupation number, $\delta E/\delta q_i$, equivalent to the orbital electronegativity,[6] and are closely related to ionization potentials and electron affinities. The energy difference between a filled and an empty orbital constitutes a direct estimate of the arithmetric mean value of the corresponding $S_0 \rightarrow S_1$ and $S_0 \rightarrow T_1$ uv-transitions.

The active orbitals of the norbornadiene-cycloheptatriene rearrangement, the rate determining step of which is a 1,3-sigmatropic shift,[7] are the filled σ-orbital localized mainly on the migrating carbon atom and the empty π_g^*-orbital. The linear correlation between the known activation energies of this system[7] and $\Delta\varepsilon$, the energy difference between the active orbitals calculated with the HAM/3 method, is shown in Figure 1.

Similarly, the active orbitals of the Cope rearrangement are identified as the σ-orbital constituting the single bond to be broken and the π_g^*-orbital. The linear correlation between experimental activation energies[8] and calculated orbital energy differences ($\Delta\varepsilon$) is shown in Figure 2.

For the Diels-Alder reaction, the active orbitals are the π_2 orbital of the diene and the π^* orbital of the dienophile. The correlations between activation energies[9] and active orbital energy differences for the reaction of cyclopentadiene and 9,10-dimethylantracene, respectively, with a series of dienophiles are shown in Figures 3 and 4. In this case, $\Delta\varepsilon$ is obtained through spectroscopic calibration of the HAM/3-calculated value:

$$\varepsilon_{\pi_2}\ (\text{diene}) = \varepsilon_{\pi_2}\ (\text{HAM}) + \text{IP}(\text{exp}) - \text{IP}(\text{HAM})$$

$$\varepsilon_{\pi^*}\ (\text{ene}) = \varepsilon_{\pi}\ (\text{HAM}) + \text{IP}(\text{exp}) - \text{IP}(\text{HAM}) + \Delta\varepsilon_{\pi\pi^*}\ (\text{exp}) - \Delta\varepsilon_{\pi-\pi^*}\ (\text{HAM}) - \Delta\varepsilon_{S-T}\ (\text{HAM})/2.$$

For the norbornadiene and Cope rearrangements, the effect of the electron-releasing substituents is to destabilize the filled active orbital, while the energy level of the empty active orbital is unaffected. In the Diels-Alder reaction, the situation is reversed. Here, the electron-withdrawing substituents of the dienophile stabilize the empty active orbital π^*.

Thus, the origin of the substituent effects in these systems is the destabilization and/or stabilization of the active orbitals of the reactants, rather than an isolated transition state effect, as is usually suggested.[1] This conclusion is consistent with the observations of linear relations between UV-transition energies and activation energies for thermal rearrangements of some cyclic olefins[10] and between diene ionization potential and log k in Diels-Alder reactions of acylaminobutadienes with methyl acrylate.[11]

The direct proportionality between the activation barrier and the active orbital energy difference demonstrated here constitutes an empirical structure-reactivity relationship reminiscent of the Hammett equation and related linear free-energy relationships.

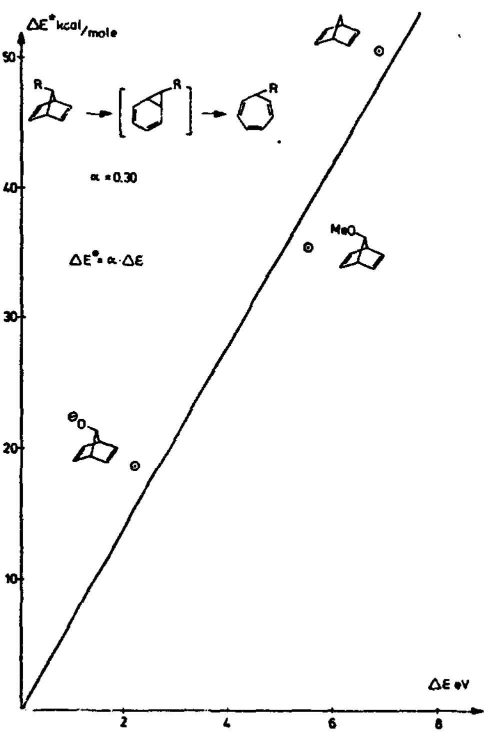

Figure 1

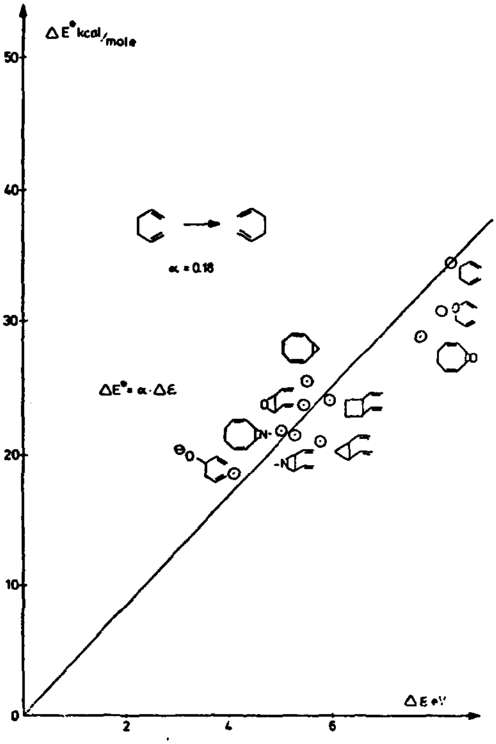

Figure 2

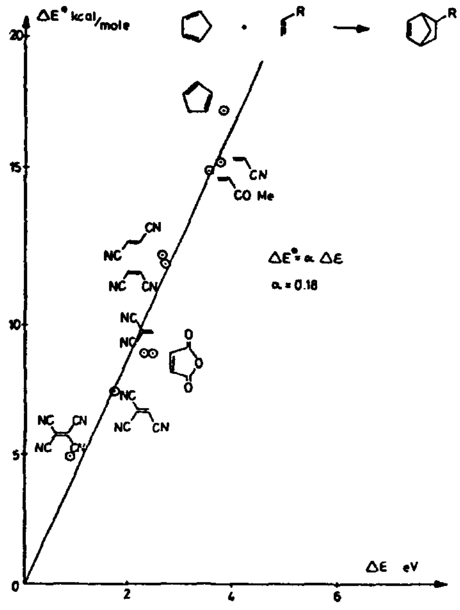

Figure 3

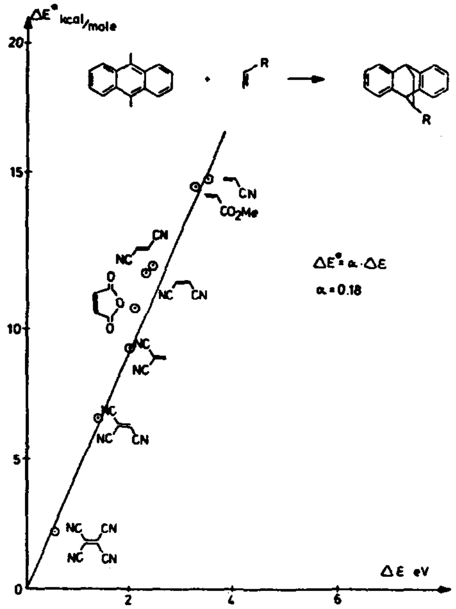

Figure 4

REFERENCES

1. Presented at the 175th ACS Meeting, Anaheim, March 12 - 17, 1978.

2. R.F.W. Bader, *Can. J. Chem.*, 40 1164 (1962); R. Sustmann, *Pure Appl. Chem.*, 40, 569 (1974); W.C. Herndon, J. Feuer, W.B. Giles, D. Otterson and E. Silber in *"Chemical Reactivity and Reaction Paths"*, G. Klopman, Ed. Wiley, New York, N.Y. (1974); K.N. Houk, *Acc. Chem. Res.*, 8, 361 (1976).

3. B.K. Carpenter, *Tetrahedron* 34, 1877 (1978).

4. This notation is preferred here to that of frontier orbitals since the active orbitals are not necessarily true frontier orbitals in the general case.

5. L. Åsbrink, C. Fridh and E. Lindholm, *Chem. Phys. Lett.*, 52, 63, 69, 76 (1977).

6. J. Hinze, M.A. Whitehead and H.H. Jaffé, *J. Amer. Chem. Soc.*, 85, 148 (1963).

7. W.C. Herndon and L.L. Lowry, *J. Amer. Chem. Soc.*, 86, 1222 (1964); R.K. Lustgarten and H.G. Richey, Jr., *J. Amer. Chem. Soc.*, 96, 6393 (1974); B. Franzus, M.L. Scheinbaum, D.L. Water and H.B. Bowlin, *J. Amer. Chem. Soc.*, 98, 1241 (1976).

8. W. von E. Doering, V.G. Toscano and G.H. Beasley, *Tetrahedron*, 27, 5299 (1971); F.W. Shuler and G.W. Murphy, *J. Amer. Chem. Soc.*, 72, 3155 (1950); W. Grimme and K. Seel, *Angew. Chem.*, 85, 514 (1973); G.S. Hammond and C.D. De Boer, *J. Amer. Chem. Soc.*, 86, 899 (1964); J.C. Pommelet, N. Maisse and J. Chuche, *Tetrahedron*, 28, 3929 (1972); J.C. Pommelet and J. Chuche, *Tetrahedron Lett.*, 3897 (1974); D.A. Evans and A.M. Golob, *J. Amer. Chem. Soc.*, 97, 4765 (1975); J.M. Brown, B.T. Golding and J. Stofko, JUN., *Chem. Commun.*, 319 (1973).

9. J. Sauer, H. Wiest and A. Mielert, *Chem. Ber.*, 97, 3183 (1964).

10. J.E. Baldwin and A.H. Andrist, *J. Amer. Chem. Soc.*, 93, 3289 (1971).

11. L.E. Overman, G.F. Taylor, K.N. Houk and L.N. Domelsmith, *J. Amer. Chem. Soc.*, 100, 3182 (1978).

(Received in UK 5 December 1978)