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THE SECONDARY α-DEUTERIUM ISOTOPE EFFECT AND THE MECHANISM OF THE DIELS-ALDER REACTION[1]

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The mechanism of the Diels-Alder reaction has received much attention recently.[2-6] The question of whether formation, isomerization, or decomposition of Diels-Alder adducts occur via a one step[2,5] or a two step[3,4,6] mechanism, has been asked most frequently. The use of the secondary α-deuterium isotope effect is especially suited to the resolution of this problem since it has already been shown[7] from the magnitude of this effect, in a similar kinetic problem, that both azo-bis-α-phenylethane and α-phenylethyl-azo-2-propane decompose by breaking both carbon-nitrogen bonds simultaneously rather than decomposing in a two step process. The mechanism of formation of the adduct can be determined, by the Principle of Microscopic Reversibility, from the mechanism of its decomposition.

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[1] Research performed under the auspices of the U.S. Atomic Energy Commission.

[2] A. Wasserman, J. Chem. Soc. 612 (1942).

[3] C. Walling and J. Peisach, J. Amer. Chem. Soc. 80, 5819 (1958).

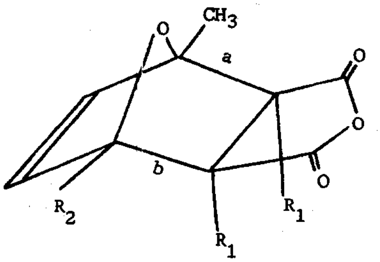
[4] R. B. Woodward and T. J. Katz, Tetrahedron 5, 70 (1959).

[5] J. A. Berson, A. Remanick and W. A. Mueller, J. Amer. Chem. Soc. 82, 5501 (1960). J. A. Berson and W. A. Mueller, J. Amer. Chem. Soc. 83, 4940 (1961); 83, 4947 (1961).

[6] M. S. Newman, J. Org. Chem. 26, 2630 (1961).

[7] S. Seltzer, J. Amer. Chem. Soc. 83, 2625 (1961); Abstracts of the 140th American Chemical Society Meeting, Chicago, Ill., September 1961, p. 71Q.

The communication of Van Sickle[8] prompts us to report our results. In the present research, the isotope effects in the retrogression of the Diels-Alder adduct (4-methyl-7-oxa-bicyclo [2.2.1.] -2-heptene-exo-5,6-dicarboxylic acid anhydride,[9] I, m.p. 75°) from maleic anhydride and 2-methylfuran, were measured. Isotopically-substituted compounds, II (m.p. 76°) and III (m.p. 75°) were prepared from maleic anhydride-d_2[10] and 2-methylfuran-5-d, respectively. 2-Methylfuran-5-d was prepared by decomposing 5-methyl-2-chloromercurifuran[11] in a D_2O-EtOD solution of DCl and D_2SO_4. The n.m.r. spectrum for each compound[12] is consistent with the structure and sites of isotopic substitution.



I: $R_1 = R_2 = H$

II: $R_1 = D$, $R_2 = H$

III: $R_1 = H$, $R_2 = D$

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[8] D. E. Van Sickle, Tetrahedron Letters, No. 19, 687 (1961).

[9] (a) K. Alder and K. H. Backendorf, Ann. 535, 101 (1938).

(b) These authors give 84° as the melting point while Rinkes[9f] gives 80°. The reason for the discrepancy probably lies in the fact that this material is so labile ($t_{1/2}$ = 28 min. at 50° isooctane) and therefore its melting point is dependent on the rate of heating.

(c) Although the adducts formed from furan, 2-methylfuran and 2,5-dimethylfuran and maleic anhydride were formulated as possessing the endo configuration,[9a] it was later shown[9d] that the adduct from furan has the exo configuration. Furthermore the spin-spin coupling constants between R_1 and R_2 indicate[8e] that (I) has the exo configuration.

(d) R. B. Woodward and H. Baer, J. Amer. Chem. Soc. 70, 1161 (1948).

(e) M. M. Anderson and P. M. Henry, Chem. and Ind. 2053 (1961).

(f) I. J. Rinkes, Rec. trav. Chim. 50, 1127 (1931).

[10] S. Seltzer, J. Amer. Chem. Soc. 83, 1861 (1961).

[11] H. Gilman and G. F. Wright, J. Amer. Chem. Soc. 55, 3302 (1933).

[12] I would like to thank Professor Ronald Breslow for the n.m.r. spectra.

The rates of decomposition of I, II, III were measured individually at 49.80 ± 0.05° in isooctane solution (1% ether) at concentrations of approximately 10^{-4} $\underline{M}$, by observing the increase of the optical density at 211 mμ as a function of time[13]; both 2-methylfuran[14] and maleic anhydride absorb strongly at this wavelength. The data give good first order plots. However, a least squares program for the IBM 704 was used to obtain first order rate constants listed in Table I. Compounds II and III were shown[10] to possess 1.90 and 0.94 atoms of deuterium, respectively. When corrected for full deuteration, the isotope effects are $k_I/k_{II} = 1.16$ and $k_I/k_{III} = 1.08$.

Table I. First Order Rate Constants for the Formation of 2-Methylfuran and Maleic Anhydride Diels-Alder Adduct

	Natural, I $k \times 10^4$, sec^{-1}	Dideuterated, II $k \times 10^4$, sec^{-1}	Monodeuterated, III $k \times 10^4$, sec^{-1}
	4.15	3.67	3.88
	4.08	3.51	3.84
	4.25	3.61	3.85
	4.14	3.58	3.83
	4.10	3.60	3.89
Ave.	4.14 ± 0.04	3.59 ± 0.04	3.86 ± 0.02

$k_I/k_{II} = 1.15 \pm 0.01$, $k_I/k_{III} = 1.07 \pm 0.01$

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[13] (a) The starting compound's initial extinction is $\log_{211m\mu} = 3.07$. That this is probably due to the pure compound and not to 2-methylfuran and maleic anhydride impurities derives from the fact that 3-methylcyclohexene-1-4,5-dicarboxylic acid anhydride, a compound with similar structure, possesses a $\log_{211m\mu} = 3.1$.[13b]

(b) Z. W. Wicks, O. W. Daly and H. Lack, J. Org. Chem. **12**, 715 (1947).

[14] H. L. Rice, J. Amer. Chem. Soc. **74**, 3193 (1952).

As shown previously,[7] the average observed secondary α-deuterium isotope effect in a "unimolecular" decomposition ($R_1R_2CDX \longrightarrow R_1R_2CD + X$, the fragments being radicals or ions) is $k_H/k_D = 1.12$ at 105° ($k_H/k_D = 1.15$ at 50°). If there are two reaction sites, each having α-deuterium atoms and both undergoing change simultaneously, the expected and observed effect is about twice as large.[7] Then in the reversion of the Diels-Alder adduct to its addends, if both bonds, a̲ and b̲, were to break simultaneously, a double isotope effect ($k_I/k_{II} \cong 1.30$) would be expected. On the other hand, if only one bond should break in the rate limiting step, an isotope effect of $k_I/k_{II} \cong 1.15$ would be found. Furthermore, if there is a two step process, labeling with deuterium at R_2 will define which of the two bonds are breaking in the slow step. The fact that there is an isotope effect, $k_I/k_{III} = 1.08$, although low, indicates that bond b̲ is breaking in the rate determining step. The effect, $k_I/k_{II} = 1.16$, appears to fall in the class of only one bond (b̲) breaking in the rate determining step. If both bonds were breaking, however, with less progress along the reaction coordinate from starting state to transition than in other reactions,[7] as might be indicated here by the low k_I/k_{III}, an effect of k_I/k_{II} as large as 1.30 might not be realized. Therefore the small effect, k_I/k_{III}, makes the interpretation of k_I/k_{II} somewhat ambiguous at this time.[15]

Further studies by the above method are being carried out on this and other adducts.

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[15] A referee has commented: "... . Bond b̲ of III would not be expected to break faster than bond a̲; if anything, the reverse would be true. Therefore, the observed isotope effect could be explained in the two-step mechanism only if there were two entirely separate transition states, one involving a̲ and one involving b̲, both of about the same energy, and both connecting the same reactants and products. Perhaps this is not impossible, but it seems less likely than the idea that both a̲ and b̲ are breaking simultaneously."

Although not likely, it is possible that during bond-b̲-breaking, the atomic movement about R_2 is different from that about R_1, the hydrogen atom adjacent to bond b̲. This would lead to the choice of a stepwise mechanism. Experiments designed to differentiate between the two interpretations are in progress.