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Registry No.—1a, 10310-21-1; 5, 64189-11-3; 6, 64189-12-4; 7 (2-propenyl isomer), 64189-13-5; 7 (1-propenyl isomer), 64189-14-6; 10 (1-propenyl isomer), 64189-15-7; 10 (2-propenyl isomer), 64189-16-8; cinnamyl alcohol, 104-54-1; *m*-trifluoromethylcinnamyl alcohol, 64189-17-9; 3-(3,4-methylenedioxyphenyl)-2-propen-1-ol, 17581-86-1; *O*⁶-(3-methyl-2-butenyl)guanosine, 64189-18-0.

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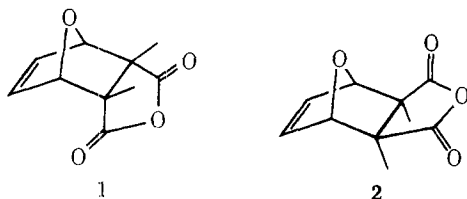
Stereochemistry of the Furan–Maleic Anhydride Cycloaddition

Martin W. Lee¹ and William C. Herndon²

Department of Chemistry, University of Texas at El Paso,
El Paso, Texas 79968

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The crystalline product from the Diels–Alder reaction of furan (F) with maleic anhydride (M) was originally formulated as endo adduct 1.² Woodward and Baer showed that the adduct actually has the exo configuration 2.³ Anet has stated⁴



that the exo isomer is initially formed about twice as fast as the endo isomer, and that the endo compound initially produced quickly disappears from the reaction mixture at room temperature.

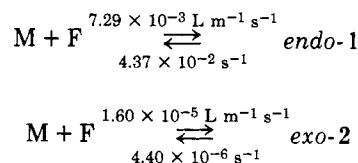
The kinetically favored formation of the exo compound is a very unusual circumstance and constitutes the only known exception to the rule of predominant endo addition⁵ in reactions where dienophiles and/or dienes are not heavily substituted.⁶ We also find that all of the usual grounds for explaining endo selectivity (maximum accumulation of unsaturation,⁷ secondary orbital interactions,⁸ primary overlap at the reaction sites,⁹ attractive dipole–dipole interactions, and dispersion forces¹⁰) are fulfilled in the furan–maleic anhydride cycloaddition. Consequently, we have reinvestigated this reaction using nuclear magnetic resonance spectroscopy.

In agreement with the previous work, the reaction of maleic anhydride with furan gives rise to the exo adduct 2: mp 125–126 °C; NMR bands at δ 6.5 (2 H, multiplet), 5.3 (2 H, multiplet), 3.2 (2 H, singlet). In acetonitrile solution at 40 °C,

initial concentrations of reactants both equal to 1.50 M, a small amount of endo-1 is initially formed and identified by its NMR spectrum: δ 6.5 (multiplet), 5.4 (multiplet), 3.9 (multiplet). However, the initial rate of formation of endo-1 is found to be larger than that for the formation of 2. At the end of 24 min the concentrations of 1 and 2 are the same, and the concentration of 2 exceeds that of 1 after that point. Endo adduct has essentially disappeared after 48 h, and the final concentration ratio of product to reactants is $[exo-2]/[M] = 1.83$ and $K = [M][F]/[2] = 0.289$ L mol⁻¹. Pure exo adduct decomposes to give only the addends. With the initial concentration of 2 equal to 0.120 M, the equilibrium concentration ratio is 0.348 and $K = 0.256$ L mol⁻¹.

At lower initial concentrations of reactants, the only initially discernable product is the endo adduct. With $[M_0] = [F_0] = 0.50$ M, 8% of the reactants are converted to 1 after 310 s, and the concentration of 1 slowly decreases after that time. Exo adduct 2 is only evident in the reaction mixture after 3000 s of reaction time. Several repetitions of all of these experiments gave congruent results.

Using the differential rate expressions directly¹¹ we find that our data yield the rate constants shown. The rate constant for formation of the endo adduct is actually almost 500 times larger than the exo adduct formation rate constant. Assuming comparable entropies of activation, this rate constant difference corresponds to an activation energy difference of 3.8 kcal favoring the endo adduct. The exo adduct is, however, 1.9 kcal/mol more stable than the endo adduct. Since the formations of both adducts are reversible, the exo adduct is eventually the final isolated product.



With these results, the furan–maleic anhydride reaction can be placed within the typical kinetic and thermodynamic pattern for Diels–Alder reactions.^{5,12}

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Registry No.—1, 64113-63-9; 2, 64161-68-8; maleic anhydride, 108-31-6; furan, 110-00-9.

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