puter-based schemes for establishing the topology of the molecular framework. If necessary, this connectivity information could be supplemented by similar measurements based on long-range couplings.[2] We suggest that the proposed technique could be a powerful aid to structure determination in cases where specific isotopic enrichment is not feasible.

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The Principle of Cooperativity in Asymmetric Induction: A Demanding Test for Concertedness

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The requirement for orbital symmetry conservation in concerted reactions is such a powerful and general one ("Violations. There are none!")[1] that its scope has been extended through topological considerations to a host of systems which lack formal symmetry but whose stereochemistry indicates concert.[2] More recently, the existence of concertedness at all has been questioned by a revisionist school which has invoked instead a relative rate effect which produces the stereospecific fingerprint of concertedness only through the fast collapse of intermediate biradicals.[3] Attempts to resolve this controversy have relied largely on circumstantial kinetic data, particularly the existence of large negative activation entropies. We now report the use of chiral prosthetic groups as direct probes of the geometry of the transition state of the Diels-Alder reaction and demonstrate that the cooperativity in asymmetric induction achieved is a direct result of the concertedness of the reaction.

Controversy surrounding the Diels-Alder reaction hinges on whether the incipient σ bonds are formed simultaneously or sequentially. The essential distinguishing feature of the two mechanisms is the nonequivalence of the two ends of the dienophile for the nonconcerted mechanism and the equivalence of the two ends for the concerted mechanism. Our approach was to probe for the geometry of the transition state by using one or two chiral groups at the ends of the dienophile and to test for the degree of asymmetric induction induced in each case. As a test case, we chose the cycloaddition of 1,3-diphenylisobenzofuran to dialkyl fumarates. The geometry of the transition state for the concerted reaction is illustrated in Figure 1. The two alkyl moieties are held sufficiently far apart by the rigid fumarate backbone that they can rotate independently. One becomes the exo substituent, the other endo. We now consider the effect on the transition state leading to enantiodifferentiation of replacing one, then two, methyl groups with an *l*-bornyl group. First, for the concerted reaction the differences in activation enthalpies for enantiodifferentiation when two chiral groups are present should be the arithmetic sum of differences for the individual chiral groups. This is analogous to additivities in isotope effects for a similar system.[4] Second, the entropy contribution, which is often more important in determining asymmetric induction,[5] will be given by $R \ln (P_{exo}P_{endo})$, where P_{exo} and P_{endo} are the probabilities for enantiodifferentiation for exo and endo singly substituted transition states. Since the entropic effects will also be additive, we have the important result that the difference in activation free energies themselves will be additive and the relative rate of enantiomer formation k_α/k_β in the presence of two chiral groups will be the product of the rates in the presence of one chiral group (see eq 1). For the non-

$$\frac{k_\alpha}{k_\beta} = \frac{k_{\alpha 1}}{k_{\beta 1}}\frac{k_{\alpha 2}}{k_{\beta 2}} \qquad (1)$$

concerted reaction, moreover, the lack of equivalence of the two ends implies that their energy effects on asymmetric induction will be nonadditive. We call this linear free energy relationship the principle of cooperativity in asymmetric induction. This concept is similar to the cumulative effects observed for methyl substitution on solvolytic reactions involving symmetric transition states.[6] However, severe steric and electronic interactions introduce second-order effects which may prevent this relationship from holding rigorously in such cases.

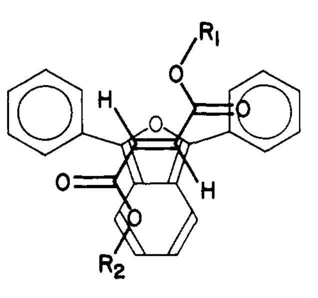
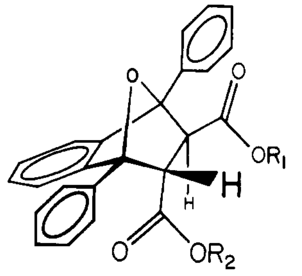


Figure 1. Diels-Alder transition state.



1, $R_1 = R_2 = CH_3$
2α, 2β, $R_1 = R_2$ = bornyl
3αexo, 3βexo, R_1 = bornyl, $R_2 = CH_3$
3αendo, 3βendo, $R_1 = CH_3$, R_2 = bornyl

Figure 2. Cycloaddition products.

Table I. Chemical Shifts and Relative Intensities of Exo Protons

compound	chemical shifts, ppm (rel intens)
1	4.34
3α, β (endo)	4.17 (0.47), 4.36 (0.72)
3α, β (exo)	4.43 (0.71), 4.45 (1.0)
2α, β (exptl)	4.25 (0.48), 4.48 (1.0)
2α, β (calcd)	4.26 4.47

Table II. Product Ratios

		2α/2β	
3α/3β (endo)	3α/3β (exo)	exptl	pred
1.53	1.41	2.08	2.16

The reaction of dimethyl fumarate with 1,3-diphenylisobenzofuran produced the Diels-Alder product **1** in quantitative yield. The reaction of dibornyl furmarate produced both diastereomers **2α** and **2β** in a 67:33 ratio, while the reaction of methyl bornyl fumarate gave a mixture of all four possible diastereomers **3** (see Figure 2). Fortunately, it was possible to relate the pair

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of diastereomers from the methyl bornyl adduct to the corresponding dibornyl diastereomer by simple consideration of chemical shift additivities in the proton NMR spectrum.[7] Thus the chemical shift of the exo proton from diastereomer **2α** was the sum of the chemical shift of the exo proton of dimethyl adduct **1** and the incremental shift for the two corresponding methyl bornyl diastereomers **3αexo** and **3βendo**. The predicted and measured chemical shifts are given in Table I. From integration of the exo proton absorptions, it was further possible to obtain the relative yields of all isomers in each cycloaddition and thus to correlate the extent of asymmetric induction obtained with two chiral groups to that obtained with one. Multiplication of the relative rates of enantioselection for the exo and endo methyl bornyl diastereomers gave the predicted values for enantioselection in the dibornyl case for comparison with the measured values (see Table II). Within experimental error, we see that they are the same.

Cooperativity in enantioselection has several important implications. First, we have further evidence of concert in the Diels–Alder reaction. Second, the fact that the relative rates are multiplicative illustrates what happens in enzymatic systems, where the net result of many chiral centers is optical yields approaching 100%. Finally, we suggest a method for increasing optical yields in asymmetric induction for natural product synthesis. Where a concerted reaction is involved in the synthesis, we may study the effect of individual chiral prosthetic groups at different sites in the molecule and predict which combination will lead to the highest optical yield. Thus we may systematically improve asymmetric induction without relying on chance.

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(7) Such additivity properties constitute a free energy relationship not unrelated to that observed for the asymmetric induction itself.

Production of Orbitally Forbidden Products in the IR-Laser-Induced Isomerization of *cis*-3,4-Dichlorocyclobutene

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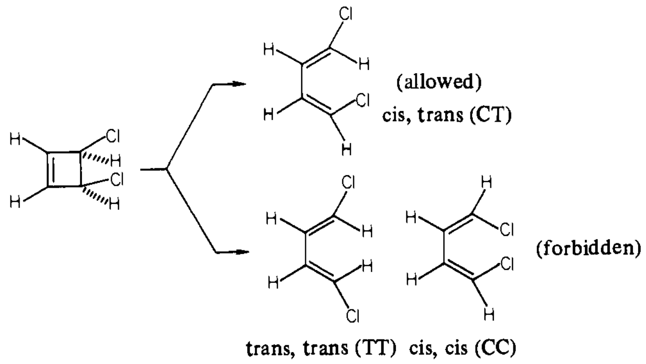
Conservation of orbital symmetry is a powerful tool for predicting the stereochemical course of concerted electrocyclic reactions.[1] Although symmetry-forbidden products can be formed, the "nonallowed" pathways generally have much larger activation energies, resulting in greatly reduced yields. One might expect, however, that vibrational excitation of the reactants in the ground electronic state by an intense infrared laser could substantially increase the yield of the symmetry forbidden products. We report here the first instance of such a laser-induced reaction, namely, the electrocyclic ring opening of *cis*-3,4-dichlorocyclobutene (DCCB) to produce the symmetry-allowed (conrotatory) *cis,-trans*-1,4-dichloro-1,3-butadiene (CT) and the forbidden (disrotatory) cis,cis and trans,trans (CC and TT) isomers:[2-5]



A pulsed CO_2 laser tuned to the 10.812 P(40) line was used to irradiate DCCB in a static Pyrex cell equipped with NaCl and quartz windows. The total yield of products was measured by UV absorption (232.5 nm), while the isomeric composition of the products was determined by GC.[6] A typical chromatogram of the reactant and product mixture is shown in Figure 1. The fractional conversion per laser pulse and the branching ratio for each product were measured as functions of laser fluence ϕ, DCCB pressure, and added buffer gas pressure. Full details of these experiments will be reported in a later publication.[7]

Our principal findings are as follows: (i) At fluences below 3.5 J/cm^2 the only observed product was the allowed CT isomer. At higher fluences the branching ratio for the forbidden products, $\Gamma = ([CC] + [TT])/([TT] + [CT])$, was found to increase linearly with ϕ, as shown in Figure 2. The ratio of CC (the most stable isomer) to TT (the least stable one) was always greater than unity and decreased with increasing fluence. Our findings are consistent with the observation by Danen et al.[8] of only the allowed product at $\phi = 3.5$ J/cm^2 in their study of the IR-laser-induced isomerization of DCCB. (ii) The fractional conversion per pulse was found to increase quadratically with neat DCCB pressure, over a range of 0.020–2.5 torr. The branching ratios, Γ and CC/TT, were essentially independent of DCCB pressure. (iii) The effects of He, Ar, N_2, and O_2 buffer gases were to decrease the fractional conversion per pulse, decrease Γ, and increase the CC/TT ratio.

A variety of tests were carried out to eliminate possible artifacts in our experiments. The branching ratios were found to vary only weakly with the number of laser pulses, N, indicating that for small N, CC and TT are not the results of secondary reactions of cold CT building up in the cell. The data points in Figure 2 are extrapolations of Γ to $N = 1$. We further noted that DCCB decayed exponentially with N, with a parallel growth of products, for as much as 70% conversion of all the DCCB in the cell. This observation rules out the possibility that energy pooling collisions between two vibrationally excited DCCB molecules contribute appreciably to the reaction mechanism. In another test, irradiation of DCCB with 8.2 J/cm^2 at 10.285 μm where DCCB absorbs very weakly produced no detectable products. This experiment rules out the possibility of surface catalysis on the cell windows.[9] We also found that at 10.812 μm, the product distribution was independent of cell dimensions.[10]

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(2) *cis*-3,4-Dichlorocyclobutene was synthesized by the method of Pettit and Henery.[5] Gas chromatographic analysis of this product after purification revealed it to be a pure compound. No detectable amounts of the *trans*-3,4-dichlorocyclobutene or the 1,4-dichlorobutadienes were present.

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