Transition States in Catalyzed and Uncatalyzed Diels-Alder Reactions. Cooperativity as a Probe of Geometry

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Abstract: The uncatalyzed Diels-Alder reaction exhibits cooperativity in asymmetric induction. That is, the enantiomeric ratio produced when the dienophile, e.g., dibornyl fumarate, contains two independent chiral moieties can be predicted on the basis of the asymmetric induction resulting when a single chiral moiety is available. When the diene is 2-fold symmetric, the bischiral ratio is the square of the monochiral ratio. The use of a Lewis acid catalyst changes the relationship and indicates a change in transition state from synchronous to asynchronous. Thus the role of Lewis acids in enhancing asymmetric induction is to increase the steric interaction at one end of the dienophile.

The intervention of concert in reactions that proceed under the control of orbital symmetry has fascinated chemists for many years. That such reactions maintain the stereochemical integrity of the reactants is by this time virtually unchallenged. Unfortunately, since concertedness is difficult to establish rigorously, stereochemical information is often used in the converse sense. That is, reactions that proceed stereospecifically are often assumed to be concerted. The fact that cis dienophiles give cis Diels-Alder adducts and trans dienophiles give trans adducts is cited as proof that the reaction is concerted. However, if we examine Figure 1, which represents the concerted (path A) and nonconcerted (path B) reaction pathways, we see that both pathways lead to stereospecific cycloaddition if the intermediate "biradical" of path B collapses to product faster than bond rotation can occur. Moreover, we see that the so-called "two-stage" mechanism,[2] in which strong correlation of the single electrons in path B leads to partial bond formation, is formally concerted. Thus we shall restrict our attention to a subset of concerted reactions, that is, those which are also synchronous.[3]

In order to differentiate between the two possible pathways, we have developed an approach that directly probes the symmetry of the transition state. If we consider the two transition states for paths A and B, we see that in path A, group E_1 and group E_2 are both attached to bond-forming centers, whereas in path B only E_2 is. Thus a group E that perturbs the transition state when close to an incipient bond will have a greater effect at one site than the other but the identical effect for the symmetrical transition state. Although in principle a substituent may perturb the system in a steric or electronic manner, we chose a perturbation that involves both minimal steric and no electronic perturbation, i.e., a chiral prosthetic group. This has led us to develop a more demanding test for synchroneity, that is, that such reactions exhibit *cooperativity in asymmetric induction.*[4] The experimental observation in such systems is that, when two (or more) chiral prosthetic groups are independently connected to the reacting centers, the asymmetric induction achieved is the arithmetic product of that induced by each group acting independently. The existence of a single transition state for formation of two bonds implies a linear free energy relationship which is more restrictive than the merely permissive observation that a reaction maintains stereochemistry. For example, the photochemical addition of *trans*-stilbene to dialkyl fumarates is stereospecific but lacks cooperativity in asymmetric induction and is therefore asynchronous.[4b]

The Diels-Alder reaction is, presumably, the sine qua non of concerted, synchronous cycloadditions.[4c] Studies by Walborsky[5] and Jurczak[6] have demonstrated that asymmetric induction can be achieved in the Diels-Alder reaction with di-*l*-menthyl fumarate and a variety of dienes, including butadiene, isoprene, and anthracene. However, none of these studies has indicated the effect of only one chiral group. We have reported that the reaction of dialkyl fumarates with 1,3-diphenylisobenzofuran (DIBF) proceeds with cooperativity in asymmetric induction.[4a] Thus the product of methyl *l*-bornyl fumarate produces the *endo*-bornyl product in an enantiomeric ratio of 1.53 and the *exo*-bornyl product in an enantiomeric ratio of 1.41. The enantiomeric ratio of 2.08 produced when di-*l*-bornyl fumarate is the dienophile is within experimental error of the 2.16 ratio predicted as the product of the individual components. This establishes that the concerted, symmetrical transition state dominates the reaction pathway, at least where symmetry is allowed. In view of the utility of asymmetric induction in probing the transition state geometry of the Diels-Alder reaction, we have extended these studies to higher temperature and have investigated the effect of Lewis acid catalysts in altering the degree of cooperativity in asymmetric induction. Furthermore, we have reinvestigated a diene system, anthracene, in which the exo and endo components are equivalent by symmetry and have studied the effect of Lewis acids in altering the degree of cooperativity. We now report the results of these studies.

Results

Diphenylisobenzofuran (DIBF). Both the absolute rates of addition and the relative rates of asymmetric induction for dimethyl, methyl *l*-bornyl, and di-*l*-bornyl fumarate with DIBF were determined. The absolute rates were measured by monitoring the disappearance of DIBF absorbance (444 nm) using excess (0.10 M) fumarate. The data gave excellent pseudo-first-order kinetics over two half-lives ($\rho = 0.9999$) and allowed a calculation of the second-order rate constant. The relative rates of asymmetric induction under the same conditions were determined using our published technique. We then calculated the bimolecular rate constant for disappearance of DIBF. The rate constants at 30.0 °C were $4.10 \pm 0.05 \times 10^{-2}$ L M^{-1} s^{-1} for dimethyl fumarate, 2.22

(1) Fellow of the Alfred P. Sloan Foundation, 1983-1985.

(2) Woodward, R. B.; Katz, T. J. *Tetrahedron* **19598** *5*, 70.

(3) At the insistence of a referee, we will reluctantly use the term "synchronous" and "asynchronous" to refer to reactions that have topologically symmetric and asymmetric transitions states. The term synchronous, which means, "simultaneous" bond formation, is imprecise and rigorously impossible except for all but a few specialized cases. Thus any steric or electronic perturbation will destroy strict symmetry. If we recognize that "simultaneous" will allow for some minor difference due to steric or small electronic effects, then the term will suffice. For a discussion of these terms, see: Gold, V. *Pure Appl. Chem.* **1983**, *55*, 1281 and ref 4d.

(4) (a) Tolbert, L. M.; Ali, M. B. *J. Am. Chem. Soc.* **1981**, *103*, 2104; (b) *Ibid.* **1982**, *104*, 1742. (c) In a paper appearing after this manuscript was submitted,[4d] Dewar and Pierini challenged this approach and its mechanistic conclusions, asserting that claims of synchroneity in the Diels-Alder reaction are unsupported by evidence. However, calculations using their approach[4e] (see text) clearly indicate that the asynchronous pathway would lead to values several standard deviations from our numbers. Moreover, their model dienes, furan and its methyl and dimethyl derivatives, violate our criterion of minimal electronic perturbation, and the evidence on synchroneity in such cases is ambiguous. (d) Dewar, M. J. S.; Pierini, A. *J. Am. Chem. Soc.* **1984**, *106*, 203. (e) Dewar, M. J. S. *Tetrahedron Lett.* **1959**, *4*, 16.

(5) Walborsky, H. M.; Barash, L.; Davis, T. C. *Tetrahedron* **1963**, *19*, 2333 and references therein.

(6) Jurczak, J. *Bull. Soc. Chem. Jpn.* **1979**, *52*, 3438.

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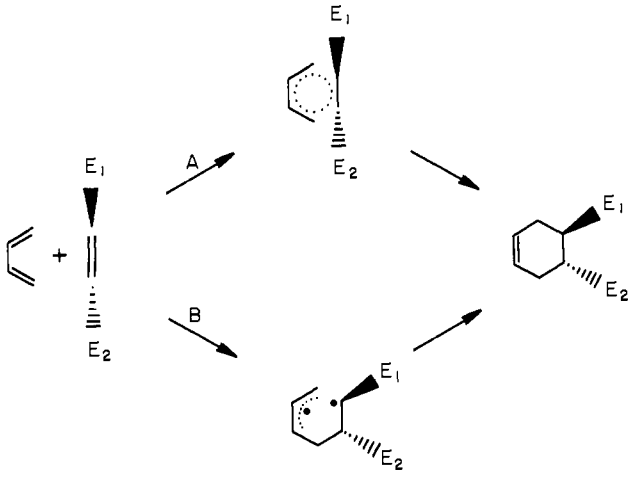

Figure 1.

Table I. Diphenylisobenzofuran[a]

fumarate	catalyst	temp[c]	enantiomeric ratio[b]
dimethyl		amb	1.0
methyl *l*-bornyl		amb	1.53 (endo), 1.41 (exo)
di-*l*-bornyl		amb	2.08 [2.16]
methyl *l*-bornyl		25 °C	1.47 (endo), 1.49 (exo)
di-*l*-bornyl		25 °C	2.17 [2.19]
methyl *l*-bornyl		50 °C	1.49 (endo), 1.43 (exo)
di-*l*-bornyl		50 °C	2.13 [2.13]
methyl *l*-bornyl		75 °C	1.52 (endo), 1.40 (exo)
di-*l*-bornyl		75 °C	2.13 [2.13]
methyl *l*-bornyl	$AlCl_3$ (1 equiv)	amb	1.20 (endo), 1.59 (exo)
di-*l*-bornyl	$AlCl_3$ (1 equiv)	amb	1.96 [1.96]
methyl *l*-bornyl	$AlCl_3$ (2 equiv)	amb	1.09 (endo), 1.92 (exo)
di-*l*-bornyl	$AlCl_3$ (2 equiv)	amb	1.89 [2.09]
methyl *l*-bornyl	$AlCl_3$ (3 equiv)	amb	0.87 (endo), 1.33 (exo)
di-*l*-bornyl	$AlCl_3$ (3 equiv)	amb	1.41 [1.16]

[a] All reactions were run in anhydrous C_6H_6. [b] Numbers in brackets represent predicted ratios. [c] amb = ambient temperature.

$\pm 0.05 \times 10^{-2}$ L M^{-1} s^{-1} for methyl bornyl fumarate, and 1.17 $\pm 0.05 \times 10^{-2}$ L M^{-1} s^{-1} for dibornyl fumarate.

The ratios of asymmetric induction for both endo and exo products, as well as the dibornyl adduct were determined at three temperatures in a thermostated (±0.02 °C) water bath. The ratios were, within experimental error, temperature independent.

The use of Lewis acid catalysts greatly accelerated the rate of cycloaddition with DIBF. Thus addition of DIBF to a solution of a dialkyl fumarate containing an equivalent of a Lewis acid catalyst yielded products identical with those from the uncatalyzed reaction, as well as products (ca. 10–30%) resulting from dehydration of the primary products, i.e., 1,4-diphenylnaphthalene-2,3-dicarboxylic acid esters. The rate of disappearance of DIBF exceeded the capacity of our kinetic apparatus; i.e., the rate was enhanced by at least 2 orders of magnitude. This rate enhancement also altered the diastereomeric ratios as a function of catalyst concentration. Surprisingly, the magnitude of the induction did not depend upon catalyst identity—$AlCl_3$, $EtAlCl_2$, $BF_3 \cdot Et_2O$—but was subject to variability due to product decomposition. The asymmetric induction obtained for each fumarate is listed in Table I.

Anthracene. The cycloaddition of anthracene and dimethyl fumarate proceeded sluggishly at room temperature but at a satisfactory rate in refluxing xylene. All uncatalyzed reactions of anthracene, therefore, were carried out in this solvent. Reaction with dimethyl fumarate, methyl *l*-bornyl fumarate, di-*l*-bornyl fumarate, methyl *l*-menthyl fumarate, and di-*l*-menthyl fumarate all proceeded in nearly quantitative (>95%) yield and gave, upon hydrolysis and reesterification with methanol, a single product, dimethyl bicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate (Figure 2). This product was identified on the basis of its melting point (107–110 °C (lit.[7] mp 107–108 °C)) and spectral data. Treatment of a $CDCl_3$ solution of the diester with the chiral shift reagent tris(3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato)-europium(III) led to a splitting of the methyl resonances in the proton NMR spectrum and allowed a ready determination of the enantiomeric ratios. The enantiomeric ratios for each dienophile are reported in Table II.

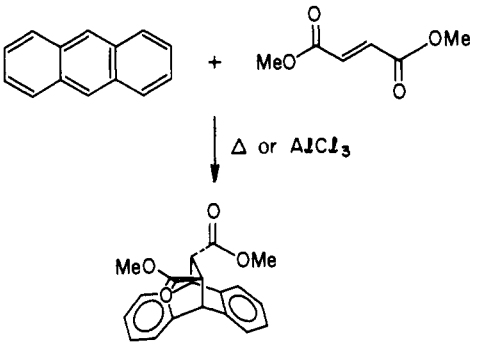

Figure 2.

Table II. Anthracene Cycloadditions[a]

fumarate	solvent	catalyst	temp[c]	diastereomeric ratio[b]
dimethyl	xylene		reflux	1.0
methyl *l*-bornyl	xylene		reflux	1.25
di-*l*-bornyl	xylene		reflux	1.53 [1.56]
methyl *l*-menthyl	xylene		reflux	1.18
di-*l*-menthyl	xylene		reflux	1.36 [1.39]
methyl *l*-bornyl	CH_2Cl_2	$AlCl_3$ (1 equiv)	amb (31–32 °C)	2.18
di-*l*-bornyl	CH_2Cl_2	$AlCl_3$ (1 equiv)	amb (31–32 °C)	2.91 [4.75]
methyl *l*-menthyl	CH_2Cl_2	$AlCl_3$ (1 equiv)	amb (31–32 °C)	3.94
di-*l*-menthyl	CH_2Cl_2	$AlCl_3$ (1 equiv)	amb (31–32 °C)	4.65 [15.5]

[a] All adducts except dimethyl fumarate adduct were hydrolyzed and estrified to the dimethyl derivative and tris[3-((heptafluoropropyl)hydroxymethylene)-*d*-camphorato]europium(III) was used to determine the enantiomeric excess. [b] Numbers in brackets represent predicted ratios. [c] amb = ambient temperature.

Addition of Lewis acid catalysts greatly accelerated the cycloaddition reaction and allowed the use of room temperature and methylene chloride solvent. The asymmetric induction was also greatly enhanced by the use of catalyst, leading to enantiomeric ratios approaching 5.0 (see Table II).

Discussion

Uncatalyzed Diels–Alder Reaction and the Origin of Cooperativity in Asymmetric Induction. By consideration of the asymmetric induction leading to exo and endo products for the addition of methyl bornyl fumarate to DIBF, we are able to predict the diastereomeric ratios for dibornyl fumarate cycloaddition by simple multiplication. Significantly, cooperativity is maintained at all temperatures. At 25 °C, the predicted α/β ratio (see Table I) is 2.19 (cf. 2.17), at 50 °C, 2.13 (cf. 2.13), and at 75 °C, 2.13 (cf. 2.13). In the case of anthracene, the exo and endo adducts are equivalent by symmetry (Figure 3). Thus we need only consider the square of the monomethyl fumarate inductions. Again, cooperativity is clearly in evidence. The predicted ratio

(7) Bachmann, W. E.; Scott, L. B. *J. Am. Chem. Soc.* **1948**, *70*, 1458.

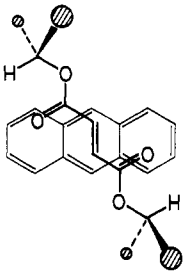

Figure 3.

for dibornyl fumarate cycloaddition, 1.56, was within experimental error of the observed ratio, 1.53. Similarly, the predicted ratio for dimenthyl fumarate cycloaddition, 1.39, was within experimental error of the observed ratio, 1.36 (see Table II).

The relative insensitivity to temperature of the diastereomeric ratios from the cycloaddition of dialkyl fumarates to DIBF implies that the difference in activation enthalpy for each diastereomeric pair is zero. Thus the diasterodifferentiation is entropic in origin, in accord with most evidence on asymmetric induction,[8] although in at least one case enthalpic effects were in evidence.[9] The maintenance of cooperativity at all temperatures implies an additivity of entropic effects. As we have previously observed, such an additivity will result for a synchronous reaction if the distribution of conformations of one prosthetic group leading to reaction is independent of the other. For dialkyl fumarates, for which the alkyl groups are separated by a relatively rigid fumarate moiety, we might expect such an independence of conformational distributions. Thus the probability of formation of one enantiomer is the product of probabilities of the two groups acting independently, i.e., the entropies are additive.[4]

Cooperativity effects leading to additivities for free energy terms are not solely observed for asymmetric induction. For the microscopic reverse of the Diels–Alder cycloaddition to anthracene, the cycloreversion of dibenzo[2.2.2]octadiene, Taagepera and Thornton observed that deuterium substitution of the four bridge protons increased the rate by a factor of 1.17, i.e., the square of the rate of substitution of only two protons, 1.08.[10] Clearly here the effect on the activation energy is enthalpic in origin, but the small magnitude of this secondary isotope effects limits its applicability. Cooperativity effects have also been invoked to rationalize the symmetry of transition states in solvolytic reactions. For example, the relative rate of solvolysis of esters of 2,4-dimethyltricyclo[3.2.1.$0^{2,4}$]octan-8-ol compared to the unsubstituted tricyclooctyl esters should be the square of the relative rate of solvolysis of the monomethyl derivative.[11] This, within experimental error, is the observation.

Cooperativity might be anticipated in cases for which steric hindrance decreases the reaction rate. Provided a bulky group does not significantly distort the transition state, the arguments for relative rate inhibition for symmetric transition states still apply. Considering path B in Figure 1, we see that a bulky group at the distal, nonreacting, end E_1 should have little effect on the relative rate but a significant effect at the proximate (bond-forming) end. For path A, again the two effects are identical by symmetry, and the relative rate for two bulky groups should be the square of that for one. Ignoring the asymmetric induction, a bornyl group is appropriately bulky, and we may use the absolute rates obtained from our kinetic measurements as a test for this model. In fact, relative rate upon replacement of one methyl group is 0.54 and for replacement of both, 0.29. The latter figure is equal to 0.54^2 or 0.29. We see then, that cooperativity effects involving steric hindrance can also be employed as mechanistic tools, although of necessity the measurement of absolute, as opposed to relative, reaction rates is required.

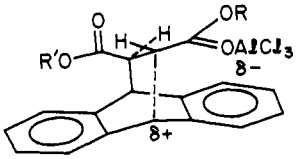

Figure 4.

Lewis Acid Catalyzed Diels–Alder Reaction. The mechanism of the catalyzed Diels–Alder reaction has been the subject of some controversy. On the one hand, the role of the catalyst may be merely to lower the energy of the LUMO of the dienophile and increase the interaction between the frontier orbitals, thus lowering the transition state without affecting its geometry.[12] The use of $AlCl_3$ in catalyzing the addition of dimethyl fumarate or dimethyl maleate has been found not to alter the stereospecificity of their addition to anthracene,[13] for instance, and thus provides circumstantial evidence in favor of concert. On the other hand, the effect of a catalyst may be to polarize the dienophile and to produce a nonsymmetric transition state. Calculations by Houk demonstrate that when Lewis acid catalysis is modeled by protonation of a prototype dienophile, an enone, the enone is polarized in such a way that the incipient bond order is increased at one end and decreased at the other end of the ethylenic carbons of the dienophile.[12] Indeed, Lewis acid catalysis of the cycloaddition of 2-phenylcyclohex-2-enone to butadiene produces, in addition to the normal cyclohexene adducts, new products reflecting a Friedel–Crafts-like transition state.[14] In this case, however, the dienophile is one that is unreactive without catalysis.

Our results enable us to distinguish among these possibilities. For the cycloadditions to DIBF, increasing amounts of Lewis acid catalyst produce a lowering, then inversion, of the diastereoselectivity leading to the *endo*-bornyl product, while raising the diastereoselectivity of the *exo*-bornyl product. The cooperativity also begins to disappear. These results are consistent with an increasingly polarized transition state. Unfortunately, the ambiguities associated with product dehydration and the eight possible transition states leading to product formation—e.g., does the catalyst always complex with the carbomethoxy or always complex exo?—make a definitive analysis in this case impossible. For the anthracene case, however, the near quantitative yields, stability of products, and symmetry of the diene allow a clearer analysis. For both menthyl and bornyl prosthetic groups, use of the catalyst leads to a marked increase in diastereoselectivity. However, virtually all of the diastereoselectivity occurs with the first chiral group, i.e., the cooperativity vanishes. Moreover, the greatly *increased* diastereoselectivity implies a much closer approach of the chiral end E_2 to the diene while the *decreased* diastereoselectivity at the other (presumably $AlCl_3$-complexed) end is consistent with a highly polarized transition state (Figure 4), in which the degree of partial bond formation, if any, is unknown. Thus *this Diels–Alder reaction is asynchronous in a system known to be stereospecific*!

Cooperativity in Asymmetric Induction Leading to Ambiguous Results. The principle that synchronous reactions exhibit cooperativity in asymmetric induction derives directly from transition state theory and is confirmed by our experiments. The contrapositive, that reactions do not exhibit cooperativity are asynchronous, is also true and has been confirmed by experiment using both the catalyzed Diels–Alder reaction and a photochemical cycloaddition. The converse, that reactions which display cooperativity are synchronous, is a more difficult principle to establish, since clearly such a conclusion depends upon the quality of the experimental data and the corresponding experimental error. Therefore, we find it useful to examine the possibility that an asynchronous reaction could still yield cooperativity effects leading

(8) Izumi, Y.; Tai, A. "Stereo-differentiating Reactions"; Academic Press: New York, 1977.
(9) Helmchen, G.; Schmierer, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 205.
(10) Taagepera, M.; Thorton, E. R. *J. Am. Chem. Soc.* **1972**, *94*, 1168.
(11) Gassman, P. G.; Chasman, J. N., Reus, W. F., III; Battiste, M. A.; Haywood-Farmer, J. *J. Org. Chem.* **1979**, *44*, 2814.
(12) Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4092. Houk, K. N.; Strozier, R. W. *Ibid.* **1973**, *95*, 4094.
(13) Yates, P.; Eaton, P. *J. Am. Chem. Soc.* **1960**, *82*, 4436.
(14) Thompson, H. W.; Melillo, D. G. *J. Am. Chem. Soc.* **1970**, *92*, 3218.

to an erroneous assumption of a synchronous pathway.[4c]

If we consider the alternative mechanism (path B) of Figure 1, we see that there are two pathways leading to product when only one of E_1 and E_2 is chiral. One pathway places the chiral group at the proximate end of the incipient bond while the other pathway places the chiral group at the distal end. The chiral induction observed for this case depends upon the relative contribution of each path leading to product. Dewar has proposed that the rate constant for the stepwise mechanism, the limiting asynchronous case, is given by

$$k_2 = \tfrac{1}{2}(k_1 + k_3) \quad (1)$$

where k_1 and k_3 are the rate constants for the unperturbed and doubly perturbed systems, and k_2 is the predicted rate constant for the singly perturbed system. Since our enantiomeric ratios are of rate constants, it follows that the enantiomeric ratio for the monochiral case is

$$\frac{k_{2\alpha}}{k_{2\beta}} = \frac{k_{1\alpha} + k_{3\alpha}}{k_{1\beta} + k_{3\beta}} \quad (2)$$

We see that the predicted ratio for the synchronous pathway is similarly derived, i.e., since

$$k_2 = (k_1 k_3)^{1/2} \quad (3)$$

it follows that

$$\frac{k_{2\alpha}}{k_{2\beta}} = \frac{(k_{1\alpha}k_{3\alpha})^{1/2}}{(k_{1\beta}k_{3\beta})^{1/2}} = \left(\frac{k_{3\alpha}}{k_{3\beta}}\right)^{1/2} \quad (4)$$

Equation 4 is equivalent to our criterion of cooperativity and, as a relative rate, does not depend upon a knowledge of absolute rates. However, the asynchronous pathway does require such knowledge. Fortunately, the combination of diastereomeric ratios and absolute rate constants at 25 °C for the reaction of dialkyl fumarates with DIBF are available and allow a calculation of the predicted ratios from eq 2 and 4. For the stepwise case, then,

$$\frac{k_{2\alpha}}{k_{2\beta}} = \frac{2.05 + 0.80}{2.05 + 0.37} = 1.18$$

For the synchronous case,

$$\frac{k_{2\alpha}}{k_{2\beta}} = (2.17)^{1/2} = 1.47$$

This is to be compared with the actual ratio, a weighted average of 1.47 and 1.49, i.e., 1.48. Assuming a standard deviation on an NMR measurement of 5%—our precision was higher—the stepwise path is several standard deviations from the observed ratio. Equation 2 also illustrates the vale of asymmetric induction as a mechanistic tool in dealing with questions of synchroneity. Thus as the steric bulk and chiroselectivity of the alkyl group increases, leading to an enhanced induction for the synchronous pathway, the asynchronous pathway leads to an enantiomeric ratio approaching 1.0. Conversely, Lewis acid complexation with the less hindered end[15] requires that k_3 dominate eq 2, since k_1 will now incorporate an equilibrium constant reflecting complexation at the more hindered end. Thus the monochiral ratio will approach the bischiral ratio. This is exactly the observed result.

Conclusions

Asymmetric induction provides a sensitive probe of transition state geometry that can be useful when stereospecificity alone is misleading. The Diels–Alder reaction, which is stereospecific in both catalyzed and uncatalyzed conditions, is truly synchronous only when a catalyst is not available to polarize the transition state. The effect of Lewis acids in increasing the optical yields when chiral substrates are involved is to increase the steric interaction at the end distal to the catalyst, thus enhancing the diastereoselectivity. This effect is completely analogous to high differentiation observed for aldol and related condensations.[16] This double differentiation, moreover, has an origin similar to that of the concerted Diels–Alder reaction, i.e., the double differentiation is due to a multiplication of independent effects. In the aldol case, since the interacting chiral centers are not linearly independent, the effect is not a true cooperative one. We anticipate that this and other examples of multiplicative effects in asymmetric induction will stimulate further efforts in its development both as a mechanistic and as a synthetic tool.

Experimental Section

General Procedure. Materials. All solvents were ACS reagent grade (organic reagents, unless otherwise noted, were obtained from Aldrich Chemical Co., Milwaukee, WI, and were used as received). Benzene was dried by storing over calcium chloride then distilling and storing over molecular sieves (Linde 4A). Methanol was purified by distillation over magnesium and iodine and stored over molecular sieves.

Analysis. Melting points were taken on a Thomas-Hoover capillary melting apparatus and are corrected unless otherwise stated. All ^{1}H NMR spectra were recorded on a Varian EM-390 spectrometer and are reported in ppm downfield from internal tetramethylsilane (δ). When peak multiplicities are reported, the following abbreviations are used: s, singlet, d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened. The diasteromeric ratios were determined by the treatment with chiral shift reagent and integration of the diastereomeric protons by "cut and weigh" method after expansion of the appropriate spectral region. At least three independent measurements were made, and the average was taken. The standard deviation in measurement was ±2%.

Kinetic Measurements. Solutions of 0.2 M dialkyl fumarate and 0.0002 M DIBF in benzene were prewarmed in a thermostated (± 0.02 °C) water bath, which also served as the reservoir for the reaction cell. Equal volumes of the two solutions were mixed in the cell, and the disappearance of the 440-nm absorption of DIBF was monitored using a Gilford Model 250 single-beam spectrophotometer interfaced to a DEC LSI-11 based minicomputer. Within-run standard deviations were 0.001%, and run-to-run standard deviations were 1–4%. Rate constants for the pseudo-first-order decays were determined by least-squares techniques, and the bimolecular rate constants were calculated from the diluted fumarate concentration. The rate constants so calculated were, for dimethyl fumarate, $4.10 \pm 0.05 \times 10^{-2}$ L M^{-1} s^{-1}, methyl *l*-bornyl fumarate, $2.22 \pm 0.05 \times 10^{-2}$ L M^{-1} s^{-1}, di-*l*-bornyl fumarate, $1.17 \pm 0.05 \times 10^{-2}$ L M^{-1} s^{-1}.

Dimethyl 2,3-Benzo-1,4-diphenyl-7-oxabicyclo[2.2.1]hept-2-ene-5,6-dicarboxylate. To a solution of dimethyl fumarate (0172 g, 5.00 mmol) in 5 mL of benzene was added 1,3-diphenylisobenzofuran (1.35 g, 5.00 mol) in 5 mL of benzene. The mixture was stirred for 3 h at room temperature and the solvent removed by room temperature evaporation in vacuo to yield a colorless solid in 98% yield.

Spectral data: NMR ($CDCl_3$) δ 3.26 (s, 3 H, *endo*-OCH_3), 3.43 (s, 3 H, *exo*-OCH_3), 3.59 (d, 1 H, endo ring proton, 4.34 (d, 1 H, exo ring proton), 7.13–7.89 (complex, 14 H, Ar).

Anal. Calcd for $C_{26}H_{22}O_5$: C, 75.36; H, 5.31. Found: C, 75.25; H, 5.39.

***l*-Bornyl Methyl 2,3-Benzo-1,4-diphenyl-7-oxabicyclo[2.2.1]hept-2-ene-5,6-dicarboxylate.** To 1.33 g (5.00 mmol) of methyl bornyl fumarate in 15 mL of dry benzene was added 1.35 g (5.00 mmol) 1,3-diphenylisobenzofuran (1.35 g, 5.00 mmol) in 10 mL of benzene. The solution was stirred at room temperature for 12 h and the solvent removed by evaporation in vacuo at room temperature. The oily residue was chromatographed on a 30 × 2 cm silicate gel column with 5% ether in *n*-hexane as eluent to yield the Diels–Alder adduct as a colorless oil in 70% yield.

NMR spectral analysis showed the exo to endo isomer ratio to be 44:56 and the diastereomeric ratio to be 1.41 and 1.53 for the exo and endo isomer (respectively).

Spectral data: NMR ($CDCl_3$) δ 0.43–2.36 (complex, 16 H, bornyl ring), 3.30 (s, 3 H, *endo*-OCH_3), 3.49 (s, 3 H, *exo*-OCH_3), 3.59 (m, 1 H, *endo*-CHCO), 4.14–4.46 (d at 4.17, ddd at 4.33, 1 H, *exo*-CHCO), 4.59 (m, 1 H, OCHC), 7.07–8.03 (m, 14 H, Ar).

(15) An ambiguity exists about the site of complexation of the Lewis acid catalyst in the monochiral case, i.e., at CO_2Me or at CO_2R^*. An attempt to answer this question by NMR analysis of the dienophile–catalyst complex failed because of the anisotropy of the system. In any event, increased complexation at the chiral end of the dienophile at the expense of the achiral end would lead to a *decreased* asymmetric induction. The fact that the monochiral and bischiral induction are nearly equal suggest that this alternate channel is not significant, although it may be responsible for the lack of equality of the two ratios. In any event, the transition state is clearly asynchronous.

(16) Heathcock, C. H.; White, C. T.; Morrison, J.; VanDerveer, D. *J. Org. Chem.* **1981**, *46*, 1296.

Di-*l*-bornyl 2,3-Benzo-7-oxabicyclo[2.2.2]hept-2-ene-5,6-dicarboxylate. Dibornyl fumarate (0.33 g, 0.85 mmol) in 15 mL of dry benzene was treated with a solution of 1,3-diphenylisobenzofuran (0.23 g, 0.85 mmol) in 10 mL of benzene. The solution was stirred at room temperature for 24 h then concentrated in vacuo at room temperature. A viscous mass was obtained. Chromatography of the products on a 50 × 3 cm silica gel column eluted with 2% ether/*n*-hexane gave first, dibornyl fumarate. Further elution gave Diels–Alder adduct in 50% yield as a colorless oil. NMR spectral analysis showed the presence of diastereomers in a ratio of 2.08.

Spectra data: NMR ($CDCl_3$) δ 0.44–2.36 (complex, 32 H, bornyl ring protons), 3.63–3.76 (dd, 1 H, *endo*-CHCO), 4.19–4.53 (4.25 d, 4.48 d, *exo*-CHCO), 4.66 (complex, 2 H, OCHC), 7.07–8.03 (complex, 14 H, Ar).

Thermostated Diels–Alder Reactions of Dialkyl Fumarates with 1,3-Diphenylisobenzofuran. A solution of 17 mmol of dialkyl fumarate in 10 mL of benzene and another solution of 1,3-diphenylisobenzofuran (47.1 mg, 0.14 mmol) in 15 mL of benzene were placed in a thermostated (± 0.02 °C) water bath. After ca. a 30-min temperature equilibration, the dialkyl fumarate solution was added to the dibornyl fumarate solution. The reaction mixture was allowed to stand for 12 h at the bath temperature (with occasional manual stirring). The solvent was removed in vacuo at the bath temperature. NMR spectral analysis showed the presence of diastereomers in ratios listed in Table II.

Lewis Acid Catalyzed Diels–Alder Reaction of Dialkyl Fumarate with 1,3-Diphenylisobenzofuran. To 15 mmol of dialkyl fumarate in 10 mL benzene was added 0.13, 0.26, or 0.39 mmol of aluminum trichloride. The mixture was stirred for 5 min. Then 1,3-diphenylisobenzofuran (34.0 mg, 0.13 mmol) in 15 mL of benzene was added. The mixture was stirred for 1 h at room temperature and washed 3 times with 5% $NaHCO_3$ solution and 3 times with water. The organic layer was dried with anhydrous magnesium sulfate and concentrated in vacuo to yield an oil. NMR spectral analysis showed the presence of diastereomers shown in Table II.

Dimethyl 2,3:5,6-Dibenzobicyclo[2.2.2]octa-5,7-diene-*trans*-7,8-dicarboxylate. To a solution of dimethyl fumarate (0.76 g, 2.26 mmol) in 50 mL of xylene was added 0.94 g (5.3 mmol) of anthracene. The mixture was refluxed for 48 h, the solvent was removed by steam distillation, and the trace solvent residue was removed at high vacuum (≈0.1 torr). A solid mass was obtained.

NMR spectral analysis showed that dimethyl 2,3:5,6-dibenzobicyclo-[2.2.2]octadiene-*trans*-7,8-dicarboxylic was formed in >95% yield. The unreacted dimethyl fumarate was removed by sublimation. Recrystallization from methanol produced colorless crystals, mp 107–110 °C (lit.[7] mp 107–108 °C). An NMR spectrum of the adduct with the chiral shift reagent (Tris[3-((heptafluoropropyl)hydroxymethylene)-*d*-camphorato]europium(III)]) showed the presence of a racemic mixture.

Spectral data: NMR ($CDCl_3$) δ 3.38 (br, 2 H, CHCOO), 3.56 (s, 6 H, OCH_3), 4.69 (br, 2 H, benzyl), 7.03–7.53 (complex, 8 H, Ar).

Di-*l*-bornyl 2,3:5,6-Dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate. A solution of anthracene (0.59 g, 3.30 mmol), dibornyl fumarate (1.28 g, 3.30 mmol), and 50 mL of xylene was refluxed for 48 h. The solvent was removed by rotary evaporation under vacuum, steam distillation, and high vacuum (≈0.1 torr). The yield of dibornyl 2,3:5,6-dibenzobicyclo[2.2.2]octadiene-7,8-dicarboxylate was 67% by NMR.

Spectral data: NMR ($CDCl_3$) δ 0.63–2.43 (m, 32 H, bornyl), 3.39 (br, 2 H, CHCO), 4.68 (br, 2 H, benzylic), 4.76 (m, 2 H, CHO), 7.07–7.56 (m, 8 H, Ar).

Base Hydrolysis of Chiral Dialkyl 2,3:5,6-Dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate. Dibornyl 2,3:5,6-dibenzobicyclo[2.2.2]-octadiene-*trans*-7,8-dicarboxylate (1.50 g, 2.65 mmol) was treated with 70 mL of 70% methanolic potassium hydroxide, and the solution was refluxed for 6 h. The solvent was removed by rotary evaporation under vacuum. Water was added, and the mixture was extracted several times with ether to remove *l*-borneol. The aqueous layer was acidified with HCl and extracted several times with ether. The organic extracts were combined, washed with water, and dried over anhydrous magnesium sulfate. Solvent removal in vacuo yielded 1.00 g of a solid mass.

Spectral data: NMR ($CDCl_3$) δ 3.35 (b, 2 H, $CHCO_2$), 4.69 (br, 2 H, benzylic, 7.00–7.53 (m, 8 H, Ar). The hydrolysis of the other chiral ester proceded similarly.

Esterification of 2,3:5,6-Dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylic Acid. 2,3:5,6-Dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylic acid (1.00 g) from the di-*l*-bornyl ester hydrolysis was dissolved in 50 mL of freshly distilled methanol, and 3 drops of sulfuric acid were added. The mixture was refluxed for 24 h. The solvent was removed in vacuo. The concentrate was dissolved in 60 mL of ether and washed 3 times with water. The organic extract was dried over anhydrous magnesium sulfate and concentrated. The dimethyl 2,3:5,6-dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate was isolated by preparative thin-layer chromatography as a coloreless oil.

An NMR spectrum of the pure dimethyl ester from the di-*l*-bornyl adduct with the chiral shift reagent tris[3-(heptafluoropropyl)hydroxyethylene)-*d*-camphorato]europium(III) indicated a 21% enantiomeric excess (α/β = 1.53). Similarly, the dimethyl esters resulting from hydrolysis/esterification of the catalyzed and uncatalyzed reactions of *l*-bornyl methyl, di-*l*-menthyl, and *l*-menthyl methyl esters yielded the enantiomeric ratios listed in Table II.

Methyl *l*-Bornyl 2,3:5,6-Dibenzobicyclo[2.2.2]octa-2,5-diene-*trans*-7,8-dicarboxylate. A solution of anthracene (0.18 g, 1.00 mmol), methyl bornyl fumarate (0.27 g, 1.00 mmol), and 50 mL of xylene was refluxed for 48 h. The solvent was removed by rotary evaporation under vacuum and steam distillation. The remaining trace amount of solvent was removed at high vacuum (≈0.1 torr). Methyl bornyl 2,3:5,6-dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate was formed in 75% yield (NMR analysis) as a pasty solid.

Spectral data: ($CDCl_3$) δ 3.36 (br, 2 H, $CHCO_2$), 3.50 (s, 3 H, OCH_3), 4.66 (br, 3 H, benzylic acid and CHO), 7.00–7.53 (m, 8 H, Ar). Similarly prepared was di-*l*-menthyl 2,3:5,6-dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate (50% yield by NMR analysis).

Spectral data: NMR ($CDCl_3$) δ 0.50–2.23 (complex, 36 H, menthyl), 3.33 (br, 2 H, $CHCO_2$), 4.50 (dd, 2 H, CHO), 4.63 (br, 2 H, benzylic), 7.03–7.56 (m, 8 H, Ar). Also prepared in this manner was methyl *l*-menthyl 2,3:5,6-dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate (75% yield by NMR analysis).

Spectral data: NMR ($CDCl_3$) δ 0.66–2.23 (complex, 18 H, menthyl), 3.33 (br, 2 H, $CHCO_2$), 3.46 (s, 3 H, OCH_3), 4.59 (br, 3 H, benzylic and CHO), 7.00–7.56 (complex, 8 H, Ar).

Lewis Acid Catalyzed Diels–Alder Reaction of Anthracene with Dialkyl Fumarates in CH_2Cl_2. A representative reaction is as follows: To a solution of dibornyl fumarate (0.68 g, 1.70 mmol) in 20 mL of CH_2Cl_2 was added (0.23 g (1.70 mmol) of aluminum trichloride. The solution was stirred for 10 min. Anthracene (0.31 g, 1.70 mmol) was added and the solution was stirred at room temperature (28 °C) for 28 h. The reaction mixture was washed with water (2 × 20 mL), 5% $NaHCO_3$ (2 × 20 mL), and water (2 × 20 mL). The organic extract was dried over anhydrous magnesium sulfate and concentrated under vacuum. The Diels–Alder adduct was formed in >95% yield (NMR analysis).

Test for Racemization of Anthracene/Fumarate Adduct during Hydrolysis and Esterification. Dimethyl 2,3:5,6-dibenzobicyclo[2.2.2]octadiene-*trans*-7,8-dicarboxylate (100.0 mg, 65% ee) was subjected to the hydrolysis/esterification procedure described above. NMR analysis of the reformed dimethyl ester with the chiral shift reagent indicated the presence of a 65% enantiomeric excess.

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