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Diastereoselectivities In The Diels-Alder Reactions Of Cyclopentadiene With Optically Active Dimenthyl Fumarate And Menthyl Methyl Fumarate In $LiClO_4$/Ether And On Al_2O_3

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Abstract: Reactions of cyclopentadiene with (-)-dimenthyl fumarate, which yield adducts **1** and **2**, and with (-)-menthyl methyl fumarate, which yield adducts **3** through **6**, were carried out on alumina activated at different temperatures, in $LiClO_4$/ether solutions, and in other media. Various diastereoselectivities - **2**:**1**, **3**:**4**, **6**:**5**, endo:exo [(**3**+**4**) : (**5**+**6**)], and % de [(**3**+**6**) - (**4**+**5**)]/[**3**+**4**+**5**+**6**] x 100] - were determined for these reactions. The $LiClO_4$ data were analyzed using a model in which $LiClO_4$ reversibly binds to the dienophile, resulting in competing catalyzed and uncatalyzed Diels-Alder reactions. Even in approximately 5 M $LiClO_4$, there are sizable contributions from uncatalyzed reactions in all cases. Extrapolation of the data to infinite $LiClO_4$ concentration yields data for the catalyzed reactions alone; only modest diastereoselectivities are seen for the catalyzed reactions. The alumina results were unusual because the endo:exo ratios of adducts were large but % de's were small. The selectivities on alumina could not be correlated to the activity of the solid. This behavior will occur when varying numbers and types of catalytic sites are exposed to the surface on activation.

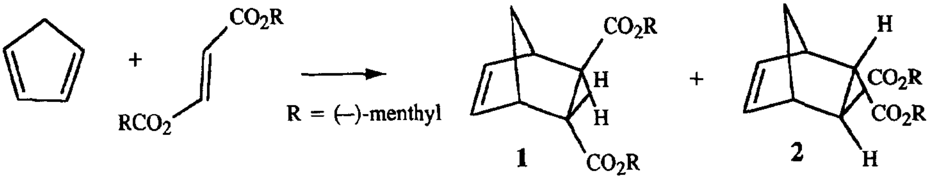
Introduction The Diels-Alder reaction is a widely studied organic reaction. It is the paradigm of a thermally allowed pericyclic reaction,[1] has been widely used in the synthesis of natural and unnatural products,[2] and has been used to probe unusual environments.[3] Even though the reaction has characteristics of a concerted process - stereospecificity arising from the reactions of *E*- and *Z*-dienophiles and *E*, *E*- and *E*, *Z*-1,3-dienes-mixtures of diastereomers (endo and endo) and regioisomers ("para" and "meta") are often generated in the reaction with suitable dienes and dienophiles.[2] Importantly, Lewis acids have a profound effect on the reaction.[2] They not only accelerate the rate of reaction, but enhance the diastereoselectivity and regioselectivity as well. The utility of a Lewis acid then depends on how effectively it carries out these tasks.

Lithium perchlorate in diethyl ether (LP/DE) has become an important medium in which to carry out the Diels-Alder and other reactions[4] in recent years. Although the effect that LP/DE has on the rate and selectivity of the Diels-Alder reaction was originally attributed to a solvent effect,[5] it is now clear that it is due to catalysis by LP,[6] which is now known to be a moderately strong Lewis acid.[7] Although data are limited, LP-catalyzed Diels-Alder reactions show enhanced endo:exo, meta:para and other types of selectivity, but the effects are modest, especially when compared to those brought about by more powerful Lewis acids.[7] Because of the importance of LP/DE in organic synthesis, a more thorough and subtle assessment of the enhanced selectivity of the LP-catalyzed Diels-Alder reaction is in order.

Surface-enhanced Diels-Alder reactions are also of current interest, with reactions on silica,[8] clays,[9] zeolites,[10] and alumina[11] being reported in recent years. Although these reactions are often used to probe the characteristics of surfaces, they also often exhibit synthetically useful selectivities and rate enhancements.

Alumina has proven to be a useful matrix on which to carry out industrially useful reactions,[12] as well as synthetically useful Diels-Alder reactions.[11] Activation of the solid by heating exposes aluminum cations to the surface[13] which catalyze the Diels-Alder reaction and give enhanced diastereoselectivity.[11] The reaction of cyclopentadiene with methyl acrylate, for example, affords endo and exo adducts in a ratio greater than 50:1 when carried out on alumina activated at 400° (400°-Al_2O_3);[11c] vastly different ratios are obtained, however, on alumina activated at both less than and greater than 400°.[11c] These subtle effects arise because the nature and number of aluminum cations exposed to the surface depend highly on activation temperature.[13] Unfortunately, how each type of aluminum cation influences the Diels-Alder reaction is not known in detail. Other surface characteristics also influence endo-exo and other types of diastereoselectivity.[11e,f] If alumina-catalyzed Diels-Alder reactions are ever to be used in synthesis, much more information on the regio-, enantio- and diastereoselectivity of the reaction will be required.

We report herein results obtained for the Diels-Alder reaction of cyclopentadiene (CP) and optically active dimenthyl fumarate (DMnF), where two diastereomeric adducts, **1** and **2**, are formed (eq. 1) and the related Diels-Alder reaction of CP and optically active menthyl methyl fumarate (MnMF), where four diastereomeric adducts, **3**, **4**, **5** and **6**, are formed (eq. 2) in $LiClO_4$/ether and on alumina. Because several selectivities can be determined for these asymmetric Diels-Alder reactions, it should be possible to assess how effective LP/DE and alumina are likely to be in enhancing selectivity in other asymmetric cycloaddition reactions.



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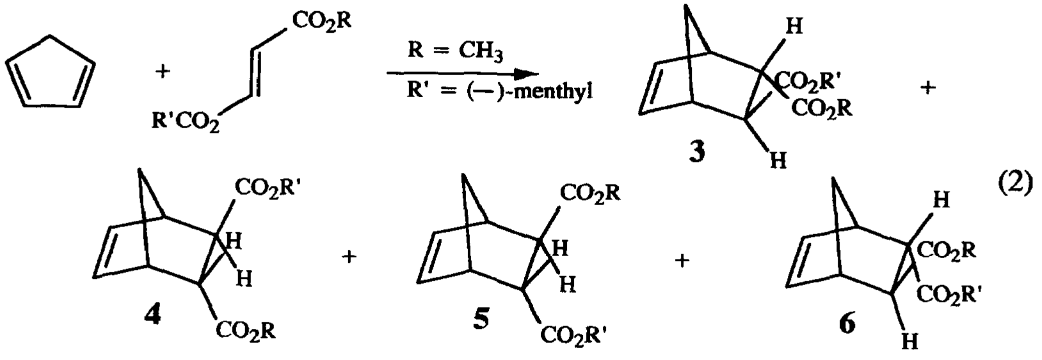


Results and Discussion

Synthesis of Dienophiles. DMnF was prepared by the Fischer esterification of fumaric acid with (-)-menthol. MnMF was prepared in three steps: (1) reaction of maleic anhydride with (-)-menthol; (2) isomerization of the resulting maleate half ester to the fumarate half ester using Br_2 and light; and (3) alkylation of the fumarate half ester with CH_2N_2.

Determination of Product Distribution. The ratio of adducts (2:1) obtained from the reaction of CP with DMnF was determined directly by high field ^1H NMR spectroscopy; the vinyl protons of 1 and 2 have different chemical shifts. Where comparisons of the present work to that published previously are possible, the ratios are identical within experimental error.[14,15]

The relative percentages of 3 through 6 obtained from the reaction of CP with MnMF were determined by a combination of high field ^1H NMR spectroscopy (3+4:5+6) and GC/MS (4+5:3:6), and are based on the work of Yamamoto.[16]

Diastereoselectivities. Let us begin by examining the behavior of the reaction of DMnF with CP in a variety of common solvents and in the presence of widely used Lewis acids. The reported diastereoselectivities (Table I) derive from the present study and previously published work. Error limits are shown where known. These data provide a perspective to those reported later for reaction 1 in $LiClO_4$/ether and on alumina.

The first seven entries of Table I deal with the effect that solvent has on the diastereoselectivity of reaction 1. The solvent effect is modest, with diastereomeric ratios lying within a few percent of 1.0. Interestingly, there is no obvious correlation between these solvent effects and a variety of solvent parameters[17] including Ω, which is a solvent polarity parameter based on the endo:exo ratio of adducts obtained for the reaction of CP and methyl acrylate.[18]

The diastereoselectivity of reaction 1 is, predictably, greatly enhanced in the presence of aluminum-containing Lewis acids (Table I, entries 8-12), with 2 being the predominant product. The best results were obtained with Et_2AlCl in toluene at two temperatures, with the better

Table I. Diastereoselectivity in the Reaction of CP and DMnF. Solvent and Lewis Acid Effects.

entry	solvent	Lewis acid	reaction temperature	2:1
1	acetone	none	20°	1.06 ± .01[a]
2	toluene	none	25°	1.04[b]
3	dioxane	none	20°	1.03[a]
4	ether	none	22°	0.95 ± .03[c]
5	methylene chloride	none	20°	0.93 ± .01[a]
6	methylene chloride	none	22°	0.92 ± .03[c]
7	neat	none	22°	0.93[d]
8	ether	$AlCl_3$	22°	2.24[d]
9	methylene chloride	$AlCl_3$	22°	4.99 ± .14[c]
10	toluene	Et_2AlCl	-20°	21[b]
11	toluene	Et_2AlCl	-70°	2.0×10^2 [b]
12	methylene chloride	$AlCl_3{\cdot}Et_2O$	-70°	2.5[a]

a) reference 14. b) reference 15. c) present work. d) reference 11f.

diastereoselectivity being obtained at the lower of the two reaction temperatures.[19] Solvent is also important here. Aluminum chloride-catalyzed reaction 1 affords a higher ratio of **2**:**1** in methylene chloride than in ether.

The relative yields of **3**–**6** obtained from several catalyzed and uncatalyzed reactions of CP with MnMF are reported in Table II. All of the entries are from the present study except entries 2, 5 and 6 which describe work published earlier by Yamamoto *et al.*[16] The percent diastereomeric excess (% de) - [(**3**+**6**)-(**4**+**5**)]/[**3**+**4**+**5**+**6**] x 100 - as defined by Yamamoto,[16] and the endo methyl to exo methyl ratio (N:X), which is (**3**+**4**):(**5**+**6**), are also reported in Table II.

As was the case for the reaction of CP and DMnF, the uncatalyzed reaction of CP and MnMF in methylene chloride and ether at 22° afforded small diastereoselectivities, with the % de being in the neighborhood of –10%, with **4** + **5** being in excess, and the N:X ratio being close to one. The reaction in toluene at 80° gave similar results.[16] As expected, the catalyzed reactions (entries 4-6) yielded superior selectivities. The % de's increased significantly, now with **3**+**6** being in excess. Although the N:X ratios also went up in these cases, only the methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD)-catalyzed reaction gave a significantly enhanced N:X ratio, however. The superior results with MAD are undoubtedly a consequence of a steric effect - the catalyst probably only binds to the carbonyl oxygen on the methyl side of the dienophile - and the low reaction temperature (–78°).

The LP/DE data are also interesting. There is, firstly, no endo to exo selectivity at any of the $LiClO_4$ concentrations examined in this study. The % de's are more positive for LP/DE than in ether alone, and they go up as the concentration of $LiClO_4$ goes up. This is consistent with a scheme in which

Table II. Relative Yields of 3-6 and Diastereoselectivities for the Reaction of MnMF and CP

		relative percentage					
entry	conditions[a]	**3**	**4**	**5**	**6**	% de[b]	N:X[c]
	uncatalyzed						
1	methylene chloride	21.8	27.3	28.2	22.7	-11.0	49:51
2	toluene[d,e]	22.8	26.4	24.0	26.8	- 0.8	49:51
3	ether	22.1	27.7	26.3	23.9	- 8.0	50:50
	catalyzed						
4	$AlCl_3$/methylene chloride	35.2	18.0	14.7	32.1	+34.6	53:47
5	Et_2AlCl[d,f]	52.5	4.6	5.2	37.7	+80.4	57:43
6	MAD[d,f,g]	91.4	7.0	0.2	1.4	+85.6	>98:2
	$LiClO_4$/ether						
7	0.980 M	24.7	24.8	26.8	23.7	- 3.2	50:50
8	2.80 M	26.0	23.6	25.5	24.9	+ 1.8	50:50
9	4.60 M	26.7	24.5	24.0	24.8	+ 3.0	51:49
	Alumina						
10	RT[h,i]	30.7	29.9	20.2	19.2	- 0.2	61:39
11	200°[h]	32.0	33.9	17.4	16.7	- 2.6	66:31
12	400°[h]	34.4	36.4	13.9	15.3	- 0.6	71:29
13	700°[h]	35.4	39.3	12.4	12.9	- 3.4	75:25
14	700°[h,j]	40.7	42.4	7.8	9.1	- 0.4	83:17

a) Reactions were run at 22°C unless noted otherwise. b) % de = [(**3** + **6**) - (**4** + **5**)]/[**3** + **4** + **5** + **6**] x 100; ref. 16. c) (**3** + **4**):(**5** + **6**). d) Ref. 16. e) Reaction run at 80°. f) Reaction run at -78°. g) MAD = methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide). h) Temperature used to activate alumina. i) RT = unactivated alumina. j) Reaction run at -5°.

there are competing uncatalyzed and catalyzed Diels-Alder reactions. With low $LiClO_4$ concentrations the uncatalyzed reaction, which gives low % de's, dominates, while with larger $LiClO_4$ concentrations, the catalyzed reaction, which gives large % de's, dominates. By methods similar to those to be described below, it is possible to extrapolate the % de data to infinite $LiClO_4$ concentration and obtain the % de for the $LiClO_4$-catalyzed reaction only. The resulting value of $10 \pm 2\%$ is clearly inferior to those obtained for Et_2AlCl/CH_2Cl_2 and MAD/CH_2Cl_2 at -78° and for $AlCl_3/CH_2Cl_2$ at 22°. The N:X ratio of approximately 1 at infinite $LiClO_4$ concentration is also inferior to those obtained with the aluminum-containing Lewis acids.

The diasteromeric ratios, **3**:**4** and **6**:**5**, derived from the data for reaction 2, and **2**:**1**, derived from the data for reaction 1, are reported in Table III. The **3**:**4** ratio is, of course, a measure of the diastereomeric excess of the two endo methyl adducts and the **6**:**5** ratio, of the two exo methyl adducts. It is apparent that for the reactions run in $LiClO_4$/ether the ratios rise rapidly and approach an

Table III. Selected Diastereomeric Ratios for Reactions of CP with DmnF and MnMF.

entry	conditions[a]		2:1 exp[b]	2:1 theo[c]	3:4 exp	3:4 theo[c]	6:5 exp	6:5 theo[c]
1	methylene chloride		0.92		.799		.805	
2	$AlCl_3/CH_2Cl_2$		4.99			1.95		2.18
3	ether		0.95	.95	.797	.797	.909	.805
	$LiClO_4$/ether[d]							
4	.950 M	.980 M	1.28	1.28	.996	.994	.884	.886
5	2.80 M	2.80 M	1.37	1.35	1.10	1.08	.976	.977
6	4.50M	4.60 M	1.35	1.37	1.09	1.11	1.03	1.03
7	∞[c]			1.41		1.17		1.24
	Alumina							
8	room temp[e,f]		1.34	1.34[g]	1.03		.950	
9	200°[e]		1.40	1.40[g]	.944		.960	
10	400°[e]		1.43	1.43[g]	.945		1.10	
11	700°[e]		1.46	1.46[g]	.901		1.04	
12	700°[e,h]		1.48		.960		1.17	

a) Reactions run at 22° unless otherwise noted. b) Experimental results. c) See text for explanation. d) Column 1 = concentrations for reaction 1 and column 2 = concentrations for reaction 2. e)Temperature at which the alumina is activated. f) Room temp = unactivated alumina. g) 2:1 ratios calculated assuming $Q_1 = 1.34$, $Q_2 = 1.87$ and $a = 0.177\ M^{-1}$. See text for explanation. h) Reaction run at -5°.

asymptotic value as the concentration of $LiClO_4$ goes up. This behavior is consistent with the aforementioned model in which there are competing uncatalyzed and catalyzed reaction. This model, which can be described mathematically (see Experimental Section), yields, in the case of **1** and **2**, the following equation

$$\frac{\textit{Amount of } \mathbf{2}}{\textit{Amount of } \mathbf{1}} = \frac{Q_1 + Q_2 a\,[Li^+]}{1 + a[Li^+]}$$

where Q_1 is the ratio of **2**:**1** at zero $LiClO_4$ concentration, Q_2 is the ratio of **2**:**1** at infinite $LiClO_4$ concentration, i.e. for the catalyzed reaction, and a is a constant equal to $k_1' K_{eq}/k_1$, where K_{eq} is the equilibrium constant for the reaction of $LiClO_4$ with the dienophile, and k_1 and k_1' are respectively the rate constants for the uncatalyzed and catalyzed reactions yielding **1**. The model assumes that the dienophile and $LiClO_4$ form a single reactive 1:1 complex and ignores the contributions of higher aggregates of the two species.[20] Similar equations can also be derived for **3**:**4** and **6**:**5**. As can be seen in Table IV, the model gives theoretical ratios which agree with the experimental values within the error limits of the experiments. Limiting Q_2 (a/M^{-1}) values for **2**:**1**, **3**:**4** and **6**:**5** of 1.41 (2.58), 1.17 (1.14) and 1.24 (.233) were obtained from the model.[21]

The selectivities of the $LiClO_4$-catalyzed reactions are modest. One way to see that this is so is to compare a diastereomeric ratio for the catalyzed reaction to the uncatalyzed reaction, i.e., Q_2/Q_1. This enhancement factor, for example, is 1.48 for **2**:**1**. Thus, the $LiClO_4$-catalyzed reaction gives a 48% larger ratio than does the uncatalyzed reaction. By the same token, **3**:**4** is enhanced by 47% and **6**:**5** by 54%. Although these enhancements seem large, they are small when compared to those obtained with $AlCl_3/CH_2Cl_2$, which gives enhancements of 442%, 145% and 171%, respectively, for **2**:**1**, **3**:**4**, and **6**:**5**.

From the model one can also calculate the percentage of each reaction that is catalyzed (Experimental Section; Table IV). What is most striking about these numbers is that even at high $LiClO_4$ concentration a sizable fraction of each product is formed from an uncatalyzed reaction. This is also apparent from the published rate data for the Diels-Alder reaction of acrylonitrile (0.7M) with 9,10-dimethylanthracene (2 x 10^{-4} M) in 4.55 M $LiClO_4$ in ether where 11.2% of the reaction is uncatalyzed.[6a,22] This may be due to the fact that reactions 1 and 2, and that of acrylonitrile and 9,10-dimethylanthracene, involve particulary reactive conjugated dienes.[23] $LiClO_4$ also may not have the intrinsic rate enhancing power of Lewis acids such as $AlCl_3$ and $GaCl_3$.[23]

Table IV. Percentages of 1-6 which Derive from Catalyzed Reaction in $LiClO_4$/Ether.

	Reaction 1			Reaction 2			
$[LiClO_4]$	**1**	**2**	$[LiClO_4]$	**3**	**4**	**5**	**6**[a]
0	0	0	0	0	0	0	0
0.950	71.0	78.4	0.980	62.0	52.7	16.9	23.9
2.80	87.8	91.5	2.80	82.4	76.1	36.7	47.3
5.40	92.1	94.5	4.60	88.5	84.0	48.8	59.6

(a) Assumes Q_1 = 0.808

There were several reasons to study reactions 1 and 2 on alumina. The alumina surface, which provides an unusual environment for chemistry, may provide unusual and synthetically useful product distributions. Furthermore, as the solid is activated, a new environment is generated at each activation temperature which may provide still new product distributions. The product distributions may lastly provide insight into the nature of the surface aluminum cations which catalyze the Diels-Alder reactions. Theory and experiment suggest that the nature and number of catalytic sites change as the solid is activated. There are, for example, normal, defect, and X-sites on the surface.[13] Each of these sites should influence reactions 1 and 2 in a unique manner. Evidence has already accrued that this is so.[11c-d] Steric effects of the surface[24] itself may also influence the behavior of the reactions.

Consider the data in Table II (entries 10-14) which describe the reaction of CP and MnMF on alumina. The product distributions and diastereoselectivities, which were obtained for reaction 2 at 22°, are significantly different than for the other cases examined in the present study or those obtained by

Yamamoto *et al.*[16] Most noticeable is the fact that the percentages of 3 and 4 go up as the temperature at which the alumina is activated goes up, while the percentages of 5 and 6 correspondingly go down. The 3:4 and 6:5 ratios are also small (See Table III for ratios). The % de's are likewise quite small and do not change in a regular fashion, but the N:X ratios are large and increase for reactions run on increasingly more activated solids. The N:X ratio is even large for reactions run on unactivated solid where there are no aluminum cations exposed to the surface. Reaction 2 was repeated at -5° on alumina activated at 700° (entry 14), where the largest N:X ratio was obtained, to see if the N:X ratio could be further increased. Not only did this ratio go up, but so did the percentages of 3 and 4 and % de as well. Extrapolation of N:X to -78°,[26] where Yamamoto and his coworkers ran their reactions with Et_2AlCl and MAD,[16] afforded N:X ≈ 96:4, a value not appreciably different than that obtained by the Japanese chemists.

How is it that the N:X ratios are large for reaction 2 on alumina at 22° but % de's and 3:4 and 6:5 ratios are small, whereas all these quantities are very large for the MAD-catalyzed reaction at -78°? Temperature does not seem to be a determining factor because, although the extrapolated N:X ratio at -78° for reaction 2 on alumina is large, extrapolated 3:4 and 6:5 ratios and % de values are still small.[26]

Steric effects explain the large N:X ratios for the MAD- and alumina-catalyzed reactions. Yamamoto and coworkers have presented convincing evidence that the sterically hindered and bulky MAD catalyst preferentially binds to the methyl ester carbonyl oxygen of the dienophile to form a complex which reacts with CP to form the two endo methyl adducts, 3 and 4. The less preferential complexation of MAD to the menthyl ester carbonyl oxygen then yields a new dienophile which affords the two endo menthyl adducts, 5 and 6. A similar argument can be made for the alumina-catalyzed reactions because the catalytically active surface-bond aluminum ions are also in sterically demanding environments due to the close proximity of the "large" surface. These sites preferentially bind to the more exposed carboxyl oxygen on the methyl ester side of MnMF, thus forming complexes which favor the formation of 3 and 4.

The small 3:4 and 6:5 ratios obtained on alumina, especially when compared to the MAD-catalyzed reaction, are difficult to explain. Because MnMF and its complexes with MAD and the aluminum sites on the surface of alumina exist in a large number of potentially reactive conformers, it is not possible to pinpoint the causes of these differences at present. MO calculations may provide insight into these issues.

Consider now the data in Table III (entries 8-12) where the ratios of adducts obtained for reactions 1 and 2 on alumina are reported. The 2:1 ratio from reaction 1 is large in all cases including that for unactivated alumina and increases as the activity of the solid increases. One plausible interpretation of this trend is that, just as was the case for reactions in LP/DE, there are competing uncatalyzed and catalyzed reactions on the solid. If one assumes that the catalyzed reactions become more important as the activity of the solid increases because there are larger numbers of equivalent aluminum ions on the surface, one can fit the experimental data to the equation

$$\frac{Amount\,of\,\mathbf{2}}{Amount\,of\,\mathbf{1}} = \frac{Q_1 + Q_2 a\,(Al^{+3})}{1 + a\,(Al^{+3})}$$

where Q_1, Q_2 and *a* have their usual meaning and (Al^{+3}) is the concentration of aluminum sites in mmol/g, which is available from literature[13] provided the surface area of the alumina is known (155 m^2/g). The fit of the data is excellent (Table IV, entries 8-11), but is unfortunately fortuitous. There is evidence in the literature that related Diels-Alder reactions are entirely catalyzed when carried out on alumina activated at > 300°,[11c-f] which would not be the case here if the above model were correct. Furthermore, if this model were valid for the **2**:**1** ratios, it should also be true for the **3**:**4** and **6**:**5** ratios, and it is clearly not; there are no obvious patterns in these ratios as the activity of the alumina is increased. Although the total number of exposed aluminum ions does increase in a regular fashion as the solid becomes more activated, the nature of the sites changes in an irregular fashion.[13] When alumina is activated at ≤ 300°, only normal acid sites are created; activation at > 300° begins to generate small numbers of highly catalytically active defect sites. Because the geometry around the normal and defect sites is substantially different, these sites should influence reactions 1 and 2 in entirely different ways. Activation at still higher temperatures produces other types of Lewis acid sites which have still different catalytic properties. Until it is possible to deduce the nature and number of acid sites as a function of alumina activity, it will not be possible to interpret quantitatively the meaning of the product ratios from reactions 1 and 2.

Concluding Remarks Final comments concerning the $LiClO_4$/ether and alumina results are in order. (1) It is clear that, although $LiClO_4$ may accelerate the rates of some Diels-Alder reactions, the effect on diastereoselectivity is modest, in particular for asymmetric Diels-Alder reactions. It is not likely that $LiClO_4$-catalyzed asymmetric Diels-Alder reactions will have synthetic utility. (2) The selectivities on alumina are unusual, especially when compared to those for MAD-catalyzed reactions. One might have expected the steric environment around the aluminum ions in both catalysts to be similar. Although there is no explanantion at present for the differences in the behavior of these two catalysts, the results of the present study show again that chemistry in unusual environments will yield unusual results.[27]

Experimental Section

(–)-Dimenthyl Fumarate. A solution consisting of fumaric acid (2.32 g, 2.00 mmol), (1R, 25, 5R) -(–)-menthol (12.5 g, 80.0 mmol), 25 mL of benzene, and 1 mL on conc H_2SO_4 was refluxed for 12 hr. After cooling, the solution was washed twice with 20 mL of water, twice with 20 mL of saturated aq $NaHCO_3$, and twice again with 20 mL of water, dried ($MgSO_4$), and then the solvent removed in vacuo. Flash chromatography of the resulting residue on silica, eluting with 5% ethyl acetate in hexanes, afforded pure (–)-dimenthyl fumarate: ^1H NMR ($CDCl_3$): 6.82 δ (2H, s, vinyl), 4.81 (2H, dt, J = 4.5, 10.8 Hz, methine next to oxygen), 0.7-2.2 (36H, m, menthyl H); ^{13}C NMR ($CDCl_3$): 164.7 δ (C=0), 134.0

(vinyl), 75.4 (menthyl carbon next to oxygen), and 47.1, 40.8, 34.2 31.5, 26.3, 23.5, 22.1, 20.8 and 16.4 (remaining menthyl).

(–)-Menthyl Methyl Fumarate. A solution consisting of (1R, 2S, 5R)-(–)-menthol (6.25 g, 40.0 mmol), maleic anhydride (3.92 g, 40.0 mmol), and 100 mL of benzene was refluxed for 12 h. After cooling, the solution was extracted three times with 100 mL of saturated aq $NaHCO_3$. The combined $NaHCO_3$ extracts were cooled in an ice bath and carefully acidified with conc HCl until the solution was acidic, after which it was extracted three times with ether. The combined ether extracts were washed with water, dried ($MgSO_4$), and the solvent removed in vacuo to give monomenthyl maleic acid: ^{1}H NMR($CDCl_3$): 10.98 δ (1H, br s, COOH), 6.36 (2H, s, vinyl), 4.84 (1H, dt, J = 4.8, 10.8 Hz, methine next oxygen), 0.7-2.1 (18H, m, menthyl); ^{13}C NMR ($CDCl_3$): 166.6 and 165.9 (C=0), 133.8 and 130.3 (vinyl), 77.1 (methine next to oxygen), and 46.6, 40.2, 33.8, 31.2, 26.0 23.1, 21.7, 20.5, and 16.0 (menthyl). The solid acid was dissolved in CCl_4 and subjected to visible light (sun lamp) while a 0.6 M solution of Br_2 in CCl_4 was added. The addition was stopped once an orange color persisted. After the color disappeared, the Br_2-procedure was repeated at which time the CCl_4 was removed in vacuo, affording monomenthyl fumaric acid. ^{1}H NMR ($CDCl_3$): 11:28 δ (1H, s, COOH), 6.88 (1H, s, vinyl), 6.86 (1H, s, vinyl), 4.82 (1H, dt, J = 4.5, 10.8 Hz, methine next to oxygen), 0.7-2.2 (18H, m, menthyl); ^{13}C NMR($CDCl_3$): 170.3 and 164.4 (C=0), 136.3 and 132.6 (vinyl), 75.7 (methine to oxygen), and 47.1, 40.3, 34.3, 31.4, 26.6, 23.7, 22.2, 20.7 and 16.5 (remaining menthyl). The fumaric acid was converted into (–)-menthyl methyl fumarate by treatment with diazomethane in ether. The product was purified by flash chromatography on silica gel, eluting with 10% ethyl acetate in hexanes; ^{1}H NMR($CDCl_3$): 6.88 (2H, s, vinyl), 4.82 (1H, dt, J = 4.5, 10.8 Hz, methine next to oxygen), 3.82 (3H, s, methoxyl), 0.7-2.1 (18H, m, menthyl); ^{13}C NMR($CDCl_3$): 165.4 and 164.3 (C=0), 134.5 and 132.9 (vinyl), 75.14 (menthyl next to oxygen), and 52.3, 47.0, 40.8, 34.3, 31.6, 26.4, 23.6, 22.1, 20.6 and 16.2 (remaining menthyl).

Representative Diels-Alder Reactions on Alumina.

A. Cyclopentadiene plus (–)-Dimenthyl Fumarate on 400°-Al_2O_3. To 24 g of Brockmann neutral alumina, which had been activated at 400° by a literature procedure,[28] was added a solution of (–)-dimenthyl fumarate (1.97 g, 5.02 mmol) in anhydrous ether (50 mL). After the resulting mixture was stirred for 30 min, the ether was removed in vacuo, resulting in a free-flowing powder. To this was added dropwise by syringe 0.5 mL (6 mmol) of cyclopentadiene. After stirring the resulting solid at 22°C (± 1°) for 20 hr, it was extracted with ether. Removal of the ether in vacuo afforded a mixture of adducts (**1** and **2**), typically in about 90% yield. The ratio of adducts was determined by high field (400 MHz) ^{1}H NMR spectroscopy by integration (or cut-and-weigh) of the appropriate vinyl resonances of the two diastereomers: 5.98 δ (**2**) and 6.04 δ (**1**).

B. Cyclopentadiene plus (–)-Menthyl Methyl Fumarate on 400°-Al_2O_3. This reaction was carried out and worked up as described in part A. The reaction afforded four adducts, **3**-**6**, formed in approximately 90% overall yield. The distribution of diastereomers was determined by a combination of high field (400 MHz) ^{1}H NMR spectroscopy and GC/MS. ^{1}H NMR spectroscopy yielded the endo (**3**+**4**) to exo (**5**+**6**) ratio by integration (or cut-and-weigh) of the methoxyl resonances at 3.61 δ and 3.68 δ, respectively. GC/MS was carried out on a 25-m crosslinked polyethylene glycol-TPA capillary column at 170°: t_R(**4**+**5**) = 74.7 min, t_R(**3**) = 78.6 min, and t_R(**6**) = 81.1 min.

Representative Diels-Alder Reactions in $LiClO_4$/Ether

A. Cyclopentadiene plus (–)-Dimenthyl Fumarate in 2.8 M $LiClO_4$/Ether. A solution consisting of 15.98 g $LiClO_4$, 3.93 g of (–)-dimenthyl fumarate (10.0 mmol), 1.0 mL of cyclopentadiene (12 mmol), and 50.0 mL of anhydrous ether (total volume = 54.0 mL) was stirred at 22 ± 1° for 20 hr after which the ether was washed twice with 50 mL of water, twice with 50 mL of 5% aq $NaHCO_3$, and twice again with

50 mL of water. After drying ($MgSO_4$), the ether was removed in vacuo to give a mixture of adducts formed in 94% yield. Analysis of the mixture was accomplished by high field ^1H NMR spectroscopy as described above.

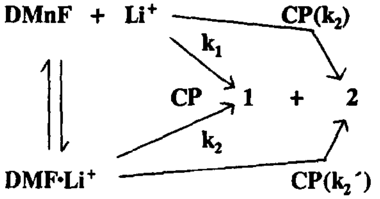
B. Cyclopentadiene plus (–)-Menthyl Methyl Fumarate in 2.8 M $LiClO_4$/Ether. The reaction was run and worked up as described immediately above. The mixture of products was analyzed by a combination of high field ^1H NMR spectroscopy and GC/MS as described previously.

Error Analysis. It is important to know how accurate the product distributions and ratios obtained for reactions 1 and 2 are because the $LiClO_4$ data must be fit to a mathematical model in order to get physically meaningful constants for the Lewis acid-catalyzed reactions.

Three unrelated methods suggest that the accuracy of the data is high. Firstly, the **2**:**1** ratios obtained for reaction 1 in methylene chloride at room temperature independently by us[11f] and Sauer,[14] and by different methods of analysis, are within 1% of each other. Secondly, the **2**:**1** ratios obtained in this study for reaction 1 on alumina and those published earlier[11f] also agree with 1-2% of each other. These two sets of data were also obtained by different methods of analysis. Thirdly, when known mixtures of methyl benzoate and methyl salicylate, esters which serve as models of the behavior of the Diels-Alder adducts, were subjected to ^1H NMR (integration and cut-and-weigh) and GC/MS analysis, the two NMR methods are precise (1 standard deviation) to within 1.4% and accurate to within 2.2%, and the GC/MS data were precise to within 0.4% and accurate to within 2.8%.

Derivation of Mathematical Equations

A. 2:1 Ratio as a Function of [Li^+]. Consider the reaction of DMnF and CP to form **1** and **2** in LP/DE by competing catalyzed and uncatalyzed Diels-Alder reactions. Assume that the catalyzed reaction occurs via a 1:1 complex of DMnF and Li^+ formed reversibly from the two components.



$$K_{eq} = ([DMnF{\cdot}Li^+])/([DMnF]\ [Li^+])$$

The rates of formation of **1** and **2** are then given by

$$\frac{d\,[1]}{dt} = k_1[CP][DMnF] + k_1{}'[CP][DMnF{\cdot}Li^+]\ and\ \frac{d\,[2]}{dt} = k_2[CP][DMnF] + k_2{}'[CP][DMnF{\cdot}Li^+]$$

Dividing the two differential equations by each other removes dt and yields (after integration)

$$\frac{Amount\ of\ 2}{Amount\ of\ 1} = \frac{k_2[CP][DMnF] + k_2{}'[CP[DMnF{\cdot}Li^+]}{k_1[CP][DMnF] + k_1{}'[CP][DMnF{\cdot}Li^+]}$$

One can remove [$DMnF{\cdot}Li^+$] from the above equation because [$DMnF{\cdot}Li^+$] = K_{eq}[DMnF][Li^+]. Thus,

$$\frac{Amount\ of\ 2}{Amount\ of\ 1} = \frac{k_2[CP][DMnF] + k_2{}'\ K_{eq}[CP][DMnF][Li^+]}{k_1[CP][DMnF] + k_1{}'\ K_{eq}\ [CP][DMnF][Li^+]} = \frac{k_2 + k_2{}'K_{eq}[Li^+]}{k_1 + k_1{}'K_{eq}[Li^+]}$$

Setting $Q_1 = k_2/k_1$ and $Q_2 = k_2'/k_1'$, the ratio of the rate constants for the uncatalyzed and catalyzed reactions, respectively, and then dividing the numerator and denominator by k_1 yields: (Amount of **2**)/(Amount of **1**) = $(Q_1 + Q_2 a[Li^+])/(1+a[Li^+])$, where $a = k_1' K_{eq}/k_1$.

One can derive similar equations for the reaction of MnMF and CP, which yields four adducts, assuming that the adducts considered in the equation derive from the same complexed dienophile. If they derive from different 1:1 complexes or admixtures of these complexes, equations of the same form are obtained but the meaning of *a* and Q_2 are different. Unlike the case of DMnF where only one 1:1 complex is possible, MnMF can yield two 1:1 complexes.

B. Percent Catalyzed Reaction as a Function of [Li⁺]. Based on the scheme in part A, one may define the fraction of **1** which is produced in a catalyzed reaction as $f_1 = k_1' K_{eq}[Li^+]/(k_1 + k_1' K_{eq}[Li^+])$. Dividing the numerator and denominator by k_1 yields

$$f_1 = \frac{(k_1'K_{eq}/k_1)[Li^+]}{1+(k_1'K_{eq}/k_1)Li^+]} = \frac{a[Li^+]}{1+a[Li^+]}$$

Thus, a knowledge of the *a* values, which are derived from the model, and $[Li^+]$ affords f_1. The fraction of **2** (f_2) is derived from $f_2 = a'[Li^+]/(1 + a'[Li^+])$, where $a' = k_2' K_{eq}/k_2 = a\, Q_2/Q_1$.

Similar equations apply to **3-6**.

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17. There is no correlation between **2**:1 and dielectric constant, donor number, acceptor number, Z values, E_T values, π and Swain's Aj and Bj values of the solvents. See Reichandt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH: Weinheim, Germany, 1988 for a discussion of these parameters.

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20. Other models were developed to fit the data. These included models with more than one 1:1 $LiClO_4$-dienophile complex and with varying admixtures of 1:1 and 2:1 complexes. These models either didn't fit the experimental data, gave physically impossible values for the adjustable

parameters, or did fit, e.g. with competing uncatalyzed and catalyzed reaction involving a 2:1 complex, in which case the simpler model shown in Appendix I was used. In any event the models which fit the data gave similar limiting values of Q_2.

21. For the **6**:**5** ratios, the value for ether ($[LiClO_4]=0$) is larger than the value for 1 M $LiClO_4$, which cannot be correct. In principle either or both of these numbers could be in error. Because the model gave physically impossible Q_2 and *a* values if the 1M value is in error, this possibility was rejected. Instead, Q_1, Q_2, and *a* were fit to the model assuming the 0.98 M, 2.8 M, and 4.6 M values are correct. This gave Q_1 = 0.805 which is significantly lower than the experimental value of 0.909. This is the only calculated number not lying within the experimental error limits of the corresponding experimental numbers.
22. Reference 6a reports other cases of larger rate enhancements which yield much smaller contributions from the uncatalyzed reactions.
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24. The Diels-Alder reactions are assumed to be irreversible and the adducts stable to epimerization. In the case of alumina, there is evidence in other Diels-Alder reactions[11c-f] that this is not always so. This is not a problem in the present examples, however. Retro-Diels-Alder reactions and epimerization reactions are very slow or non-existent on alumina activated below 400°. On the more activated solids, where these reactions (retro-Diels-Alder, epimerization) became more important, they were slowest for adducts derived from trans diester dienophiles. There is no experimental evidence that these reactions compete with reactions 1 and 2; there are no adducts formed in reaction 1 and 2, for example, with cis substituents.
25. This was accomplished by a ln(N:X) versus 1/T(K) plot.
26. Extrapolation of **3**:**4** and **6**:**5** ratios to -78° yields values of 1.3 and 1.9, respectively. From these numbers and the N:X ratio at -78°, one calculates % de = 0.1% at the same temperature.
27. The data obtained in this study can be used to determine if the $LiClO_4$-catalyzed and alumina-catalyzed reactions occur synchronously or asynchronously by application of the Tolbert-Ali test (Tolbert, L. M.; Ali, M. B. *J. Am. Chem. Soc.* **1981**, *103*, 2104 and *J. Am. Chem. Soc.* **1984**, *106*, 3806). As was observed in other cases by Tolbert and Ali, the $LiClO_4$-catalyzed and alumina-catalyzed reactions occur asynchronously. See Bains, S. Ph. D. Dissertation, University of Tennessee, 1993 for details.
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