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THE CYCLOADDITION REACTIONS OF UNSATURATED ESTERS WITH CYCLOPENTADIENE ON γ-ALUMINA

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Abstract: The Diels-Alder reaction of cyclopentadiene (CP) with methyl acrylate (MA), dimethyl maleate (DMM), and dimethyl fumarate (DMF) on alumina of varying activity has been examined. The diasteroselectivity of the reaction of CP with MA is markedly dependent on the activity of the alumina. Two factors account for these changes: (1) the nature and number of the catalytic sites on the surface, and (2) the observed reversibility of the Diels-Alder reaction on the more activated alumina. The reaction of CP with MA has been used to measure the Ω value of the surface of unactivated alumina.

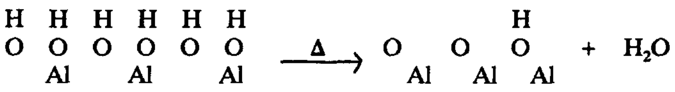
Introduction:

The Diels-Alder reaction, or 4+2 cycloaddition reaction, is one of the best methods for the construction of six-membered rings.[1] The reaction, which ordinarily involves an electron rich conjugated diene and an electron deficient alkene, is stereospecific and tolerant of various functionalities. The mechanism of the reaction has received considerable scrutiny in light of the Woodward-Hoffmann and related rules.[2] The Diels-Alder reaction can be catalyzed by Lewis acids[3] which makes it possible to perform reactions which will not occur even under the most stringent thermal conditions; the selectivities of these reactions are often greatly enhanced.

In the last several years there has been interest in carrying out the Diels-Alder reaction in unusual environments or circumstances. Reactions have been run in water[4] or $LiClO_4$/ether,[5] with antibody[6] and enzyme catalysis,[7] and on the surfaces of solids.[8-12] Often these reactions are used as probes for the environment in which the reactions occur rather than their synthetic utility.

There have been sporadic reports on the behavior of Diels-Alder reactions run on the surfaces of solids and modified solids; these include silica gel,[8] zeolites,[9] clays,[10] modified clays,[11] and alumina.[12] A variety of behaviors were observed including higher reactivity and greater selectivity as compared to solution counterparts.

Alumina provides an interesting and varied environment in which to run the Diels-Alder reaction because its surface properties vary depending on how the solid is activated. The simplest picture of unactivated alumina[13] shows a top layer of OH groups immediately above a layer of Al^{+3} cations. When the solid is heated, adjacent OH groups react to produce O^{-2} and H_2O, which is driven from the surface, thus exposing Al^{+3} to the surface (eq. 1). How much H_2O is driven from the surface depends on the temperature at which the solid is activated. Generally speaking, the higher the activation temperature, the more H_2O is removed. Activating at 300°, for example, removes approximately 50% of the OH groups,[14-15] leaving behind the remaining 50% along with oxide anions (25%) and aluminum cations (25%). Activating at 400° removes over 60% of the OH groups. The OH groups are sufficiently acidic to protonate *n*-butylamine[16] and sufficiently basic to catalyze the iodination of vinylboronic acids.[17] The oxide anions behave as bases, as attested by some of the reactions described below, and as nucleophiles;[18] the partially exposed aluminum ions behave as Lewis acids.[19] Because these species are immobile at ordinary temperatures,[20] the solid can simultaneously be a strong acid and a strong base, a situation which is not possible in solution. The surface is clearly very polar, similar in character to water or a molten salt, and capable of both donating and accepting hydrogen bonds. More sophisticated models of the surface have also been developed, such as the one due to Knözinger and Ratnasamy[15], but these will not be described here.



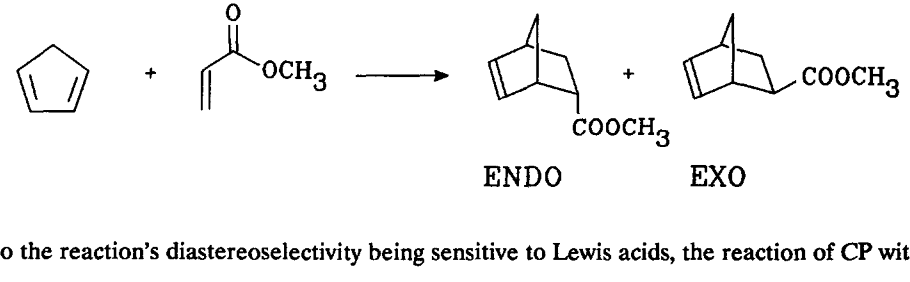
$$\begin{array}{cccccc} H & H & H & H & H & H \\ O & O & O & O & O & O \\ & Al & & Al & & Al \end{array} \xrightarrow{\Delta} \begin{array}{cccccc} & & & & H & \\ O & & O & & O & \\ & Al & & Al & & Al \end{array} + H_2O \qquad (1)$$

Because alumina is a Lewis acid unlike any seen in solution, it was of interest to determine how model Diels-Alder reactions behaved in this environment. As one might suspect, phenomena were observed which have no solution counterpart.

Results and Discussion:

Reaction of Cyclopentadiene with Methyl Acrylate

The cycloaddition reaction of cyclopentadiene (CP) and methyl acrylate (MA) (eq. 2) has been studied extensively in a variety of solvents.[21] The endo to exo ratio (N:X) of adducts generated in this reaction is sensitive to solvent polarity and is the basis for Berson's solvent polarity parameter Ω.[22] The reaction is also catalyzed by Lewis acids, which often provide enhanced diastereoselectivity.[23]



(2)

Due to the reaction's diastereoselectivity being sensitive to Lewis acids, the reaction of CP with MA was investigated on alumina of varying activities. Although surface reactions are often run as slurries of solid and solvent, all reactions were run in the absence of solvent because the Diels-Alder reaction occurs in both phases which would complicate the analysis of the results. Brockmann Activity 1 neutral alumina, which has a surface area of 155 m^2/g, was used in all cases. The alumina was activated by heating under vacuum using standard procedures.[24]

The loading of MA and CP on alumina has a significant effect on the diastereoselectivity of the reaction. When the Diels-Alder reaction was run using equimolar amounts of MA and CP on varying amounts of unactivated alumina at 50° for five hours, the results shown in Table 1 were obtained. The overall yields of the endo and exo adducts were modest due to loss of CP by dimerization. The change in the N:X ratio of adducts as a function of the weight to weight ratio of alumina to reagents is interesting. When the weight to weight ratio is ≤.4, the N:X ratio is constant at 2.9 ± 0.1. At higher weight ratios, where there is less and less MA and CP, the N:X ratio is considerably greater. Although it is difficult to calculate accurately the monolayer coverage of MA and CP on alumina, especially when they compete for the surface, it occurs between weight to weight ratios of .4 and 5. In other words, when the ratio of alumina to reagents is ≤.4, there is greater than a monolayer of reagents on the surface and the endo to exo ratio has a constant value of 2.9 ± 0.1. Interestingly, when the reaction of CP and MA is run in the absence of solvent or solid, the resulting N:X ratio of adducts is also ~ 2.9. This suggests that at high coverages of MA and CP on alumina, the reaction behaves as if there were no solid present. When there is less than a monolayer of coverage, however, the diastereoselectivity increases significantly, indicating that the reaction is occurring in a polar environment; the reaction presumably feels the full force of the polar surface. Lewis acid catalysis is not involved here because there are no aluminum ions exposed to the surface in unactivated alumina.

Table 1. The Effect of Loading of Reagents on the Diastereoselectivity of the Diels-Alder Reaction of MA and CP on Al_2O_3.

Al_2O_3:(MA + CP)[a] (w:w)[b]	% Yield of Adducts	N:X
.03	54	2.9±0.1
.05	57	2.9±0.1
.1	53	3.0±0.1
.4	55	2.8±0.1
5	60	4.5±0.2
7	57	4.2±0.2
10	62	5.8±0.3

[a]Equimolar amounts of MA and CP were used. [b]Weight to weight ratio of Al_2O_3 to organic substrates.

That unactivated alumina is polar is borne out by the data in Table 1. One measure of solvent polarity is Ω, defined by Berson, Hamlet and Mueller as log (N:X), where N and X are the endo and exo adducts formed in the reaction of CP with MA in the solvent of interest at 20°.[22] The rationalization for defining polarity in this manner can be found elsewhere.[21,22] Typical value of Ω are 0.869 for water, 0.692 for acetontrile, 0.497 for benzene, and 0.445 for triethylamine.[21] This concept should be applicable to a surface provided that it is reasonably homogeneous. Other solvent-like properties have been determined for solids.[25] Analysis of the data in Table 1, where the reactions of CP and MA were run at 50°, suggests that $\Omega \geq \log (5.8 \pm 0.3) = 0.763 \pm 0.023$, a value greater than that for ethanol ($\Omega = 0.718$). When the N:X ratio was redetermined at 20° at low concentrations of reactants [1:1 molar ratio of CP and MA; 1:10 weight ratio of (CP + MA): Al_2O_3], this yielded $\Omega = \log (5.5 \pm 0.3) = 0.740 \pm 0.024$. Unactivated alumina is thus more

and this alters N:X independent of polarity.

The effect of alumina activity on the diastereoselectivity of the reaction is interesting and unexpected. A series of reactions was run on unactivated alumina and alumina activated at 200°, 300° and 400° at two loadings of MA and CP and on alumina activated at 800° with one loading of CP and MA. All the reactions were run at 50° for five hours with the exception of the 800°-Al_2O_3 which was run at room temperature for 24 hours. The results are summarized in Table 2. As with the reactions described previously, the loading of CP and MA on the activated aluminas influences diastereoselectivity, with the lower loading providing the larger selectivity. For a given loading of CP + MA on alumina, there is a marked change in the N:X ratio of adducts on going to increasingly active alumina. The ratio increases gradually on going from unactivated alumina to alumina activated at 300°. The ratio goes up significantly on 400°-Al_2O_3, having a value of 52 for a 10:1 w:w ratio of Al_2O_3 to MA + CP. Values as high as 2.5×10^2 were seen on 400°-Al_2O_3. The reaction appears to be extremely sensitive to slight changes in the temperature at which the alumina is activated around 400°. Unfortunately, the temperature can only be regulated to ± 5° in this temperature range. Quite unexpectedly, the N:X ratio dropped to 0.93:1 when the reaction was run on 800°-Al_2O_3. This unusual pattern of behavior is not unique to the reaction of CP with MA for it was also observed in the Diels-Alder reaction of optically active menthyl acrylate with cyclopentadiene.[12d,f]

Table 2. Diastereoselectivity Observed in the Reaction of CP with MA on Alumina of Varying Activity.

	N:X Ratio	
Activation Temperature	**5.1[a]**	**10:1[a]**
Unactivated	4.5	5:8
200°	5.0	7.0
300°	6.8	10.3
400°	40	52
800°	.93[b]	

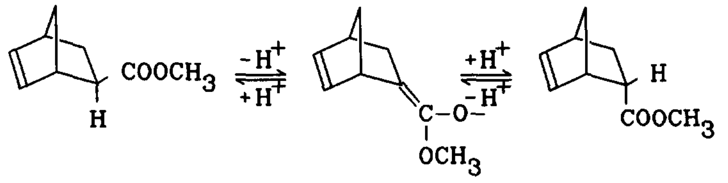
[a]Ratio of Al_2O_3: (MA + CP) (w:w). [b]The Al_2O_3: (MA + CP) (w:w) used here was 15:1.

In order to interpret these results, it was necessary to know if the adducts were stable or epimerized under the reaction conditions. Control experiments showed that epimerization reactions did not occur on alumina activated at 300° or less. On the more activated solid, however, the results were quite different. For example, epimerization occurred very slowly on 400°-Al_2O_3. The exo adduct yielded 10% of the endo adduct after 24 hours at 60°, whereas the endo adduct did not epimerize under these conditions. The epimerization reaction on 400°-Al_2O_3 is clearly much slower than the Diels-Alder reaction of MA with CP on 400°-Al_2O_3. On 800°-Al_2O_3, the results were strikingly different. When a 13.8 to 1 N:X ratio of adducts was subjected to 800°-Al_2O_3 for 5 hours at 65°, the ratio changed to 0.83 to 1[26] (eq. 3). Not only is the epimerization rapid on 800°-Al_2O_3 when compared to the reactions using 400°-Al_2O_3, a significant amount of the isomerization is due the conversion of the thermodynamically less stable endo ester to the more stable exo ester which was not observed on 400°-Al_2O_3.

$$N \overset{Al_2O_3}{\rightleftharpoons} X \qquad (3)$$

Two epimerization pathways seem plausible: one proceeding through an enolate intermediate (eq. 4) and the other via the retro-Diels-Alder reaction of N and X (eq. 5). The former pathway entails the abstraction of a proton α to the carbonyl group of N or X by a basic site on the surface followed by re-protonation of the enolate. This is a reasonable pathway because the surface of activated alumina contains basic oxide anions. The latter mechanism entails reforming CP and MA from N or X followed by cycloaddition of the fragments. This is also a reasonable pathway because retro-Diels-Alder reactions are catalyzed by Lewis acids[27] and, of course, activated alumina is a Lewis acid.

Enolate Mechanism



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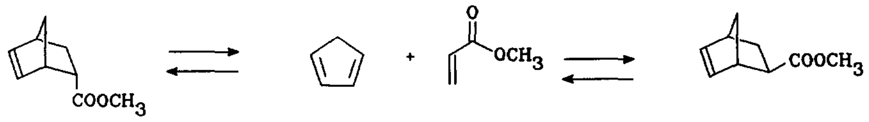
Retro-Diels-Alder Mechanism



(5)

If the enolate mechanism were operational, running the epimerization reaction on alumina in which all the surface hydrogen has been replaced with deuterium (D/Al_2O_3), a reagent we have previously prepared and used for base-catalyzed deuterium exchange,[24] would produce reactant and product which contain deuterium at the carbon α to the carbonyl group. When N was treated with 400°-D/Al_2O_3, recovered N contained no deuterium as evidenced by mass spectral analysis. When X was treated similarly, neither recovered X or formed N contained deuterium. These results rule out the enolate mechanism.

If the alternate mechanism were correct, it should be possible to trap either CP or MA formed in the retro-Diels-Alder reaction. Indeed when N was subjected to 400°-Al_2O_3 in the presence of the reactive dienophile, dimethyl fumarate (DMF), the CP-DMF adduct was generated. The most likely interpretation is that CP, generated in situ in the retro-Diels-Alder reaction, undergoes the 4+2 cycloaddition reaction with DMF.

It is notable that, when the epimerization of N or X is run on 400°-D/Al_2O_3, neither recovered N or X contained deuterium, either at the carbon α to the carbonyl group or at any position originally belonging to CP. Furthermore, when the trapping reaction with DMF was run on 400°-D/Al_2O_3, none of the recovered products contained deuterium. What makes these observations unusual is the fact that these reactions generated CP as an intermediate and, when CP was independently subjected to 400°-D/Al_2O_3, it underwent extensive deuterium exchange (eq. 6) (Table 3). In addition, when CP was treated with MA on 400°-D/Al_2O_3 both the CP dimer and N were extensively deuterated (Table 3). Thus, CP is deuterated when added to 400°-D/Al_2O_3 but is not deuterated when generated in situ by the retro-Diels-Alder reaction.

$$\text{CP} + 400°\text{-}D/Al_2O_3 \rightarrow \text{CP-d} \tag{6}$$

Another curious observation was made when CP was treated with DMF on 400°-D/Al_2O_3. Recovered CP dimer (CP_2) was extensively deuterated, while the CP-DMF adduct contained no deuterium (eq. 7) (Table 3). It appears that the Diels-Alder reaction occurs much more rapidly than the deuterium exchange on CP. This contrasts with the CP + MA reaction on the same solid where N was highly deuterated. DMF must be more reactive with CP on the alumina than MA is.

(7)

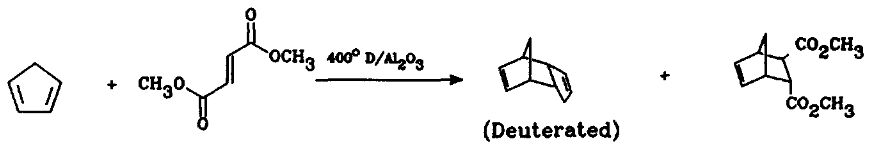


Table 3. Deuterium Incorporation in the Adducts Formed in the Reaction of CP with CP, MA and DMF on 400°-D/Al_2O_3

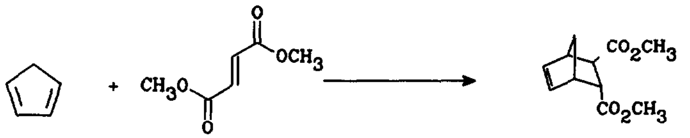
	Reaction Conditions			Deterium Incorporation into Adducts		
Reagents (mmol)	**Al_2O_3(g)**	**Time(hr)**	**Temp(°C)**	**CP Dimer**	**N**	**CP-DMF**
CP(8) + CP(8)	8	1	60	15% d_0 29% d_1 27% d_2 19% d_3 6.5% d_4 1.8% d_5 1.7% d_6		
CP(9.6) + MA(7.8)	12	1	70	53% d_0 16% d_1 16% d_2 10% d_3 3.4% d_4 1.4% d_5 0.6% d_6	49% d_0 35% d_1 12% d_2 3.5% d_3 0.3% d_4	
CP(8.3)+DMF(7.5)	16	1	60	6.6% d_0 5.6% d_1 9.2% d_2 18.6% d_3 22% d_4 22% d_5 16% d_6		100% d_0

The deuteration experiments lead to the conclusion that CP and MA, generated in the retro-Diels-Alder reaction, must re-react faster than they diffuse apart and, in the case of CP, exchange. This behavior, although very unusual, is not unique because a similar effect was observed over 35 years ago by Berson and Reynolds for the interconversion of the exo and endo CP-maleic anhydride adducts in refluxing decalin;[28] up to 45% of the exo adduct which formed from the endo adduct arose by a pathway "without dissociation into kinetically free addends."[28] It follows in the present case that, if CP and MA are never kinetically distinctive species when generated in the retro-Diels-Alder reaction, the reaction of this CP with DMF must occur by a pre-association mechanism in which trapping only occurs when DMF is in the vicinity of N or X when the retro-Diels-Alder reaction occurs. Pre-association mechanisms are well known in solution, particularly for electrophilic aromatic substitution reactions.[29]

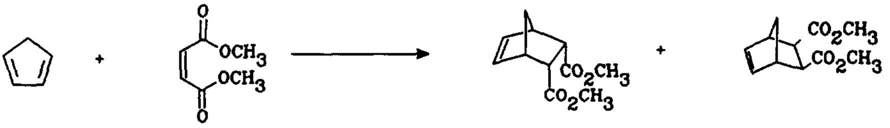
Because of the greater number of acid sites on 800°-Al_2O_3 and the enhanced acidity of some of these sites,[15] it is likely that the facile epimerization of N and X on 800°-Al_2O_3 also occurs via the retro-Diels-Alder pathway. It may be possible to utilize the 800°-Al_2O_3 as an acid catalyst in synthetically useful retro-Diels-Alder reactions, which is a topic of current interest.[27]

Diels-Alder Reaction of Dimethyl Maleate and Fumarate with Cyclopentadiene on Alumina

A reasonable extension of the chemistry described above is a study of the Diels-Alder reactions of CP with the diesters, dimethyl maleate (DMM) and dimethyl fumarate (DMF). Both of these reactions are well known in solution; DMM is less reactive and DMF more reactive than MA towards CP.[30] The cis ester, DMM, will yield both exo and endo adducts, while the trans ester, DMF, will yield a single adduct which is isomeric to the other two. The diastereoselectivity of the DMM reaction on alumina can, as in the case with MA, be used as a probe of the alumina surface. Furthermore, the three isomeric adducts could yield a richer, and perhaps more revealing, epimerization chemistry than the previously described chemistry of N and X. Also, the dienophiles, DMM and DMF, could isomerize on the solid; cis-trans isomerization of MA on alumina, of course, is not detectable.



(8)



(9)

When an equimolar mixture of CP and DMM (1 mmol each) on 10.0 g of Al_2O_3 was allowed to react at room temperature for 20 hours, a mixture of exo and endo adducts was produced (Table 4). Unlike the CP + MA reaction, where the diastereoselectivity changed in a complicated manner, the endo to exo ratio of adducts in the CP + DMM reaction increased steadily from 4.2 for a reaction run on unactivated alumina to 15.6 for a reaction run on 700°-Al_2O_3. By comparison, the reaction in methylene chloride gave an endo to exo ratio of 3.0; a ratio of 20 was obtained in CH_2Cl_2 with added $AlCl_3$. Where comparisons are possible, the selectivity of the DMM reaction is lower than for the reaction involving MA, even though the DMM reactions were run at a lower temperature where higher selectivity might be anticipated. The interpretation of the new diastereoselectivities is complicated by the fact that, on the more activated solids, the CP-DMF adduct was also formed. Similarly when the CP + DMF reaction was run on alumina, CP-DMM adducts were formed. All three isomeric adducts epimerize under the reaction conditions and, surprisingly, by three competing mechanisms.

The initial epimerization experiments were performed on 700°-Al_2O_3. When each of the three isomeric adducts was treated with this solid at 55° for 20 hours, the other two adducts were formed (Table 5). The diendo adduct had epimerized most extensively and the fumarate adduct least extensively, which reflects the anticipated stability of the isomers (fumarate > diexo > diendo). What is unusual about these results is the fact that the cis and trans adducts interconverted. If the isomerizations occurred exclusively by the retro-Diels-Alder mechanism, the two cis isomers would interconvert and the fumarate adduct would not isomerize. Other mechanisms obviously operate here. From these data alone it is not possible to say with certainty if the retro-Diels-Alder mechanism is operational.

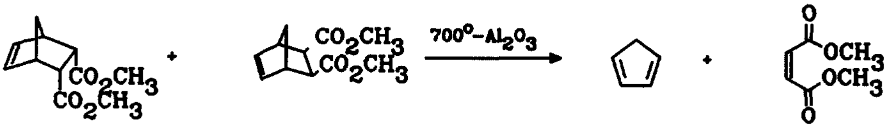
Table 4. Endo: Exo Selectivity Observed for the Reaction of CP with DMM.

Reaction Conditions	Endo:Exo
Unactivated Al_2O_3	4.2
200°-Al_2O_3	5.0
400°-Al_2O_3	7.0
700°-Al_2O_3	15.6
CH_2Cl_2	3
CH_2Cl_2 + $AlCl_3$	20

Table 5. Epimerization of CP-DMM and CP-DMF Adducts on 700°-Al_2O_3.

	Products %		
Reactant	Fumarate	Diexo	Diendo
Fumarate	95.6	2.8	1.6
Diexo	9.5	84.1	6.4
Diendo	27.6	13.2	59.1

Because CP could be intercepted by DMF when N and X were treated with activated alumina, this approach was utilized to try to determine if the retro-Diels-Alder reaction occurred during isomerization of the fumarate, diexo and diendo diesters. No trapping occurred, however, when the diesters were treated with MA, benzoquinone and TCNE on 700°-Al_2O_3. An alternate approach was then used to demonstrate that the retro-Diels-Alder reaction occurs during isomerization of these diesters on 700°-Al_2O_3. The approach took advantage of the fact that low molecular weight CP has high volatility and is not strongly adsorbed to the alumina. When a 3:1 mixture of diendo and diexo diesters was treated with 700°-Al_2O_3 in an open system where CP, if formed, could escape from the surface, DMM was formed. This result could only occur if the adducts underwent the retro-Diels-Alder reaction to form CP and DMM.



(10)

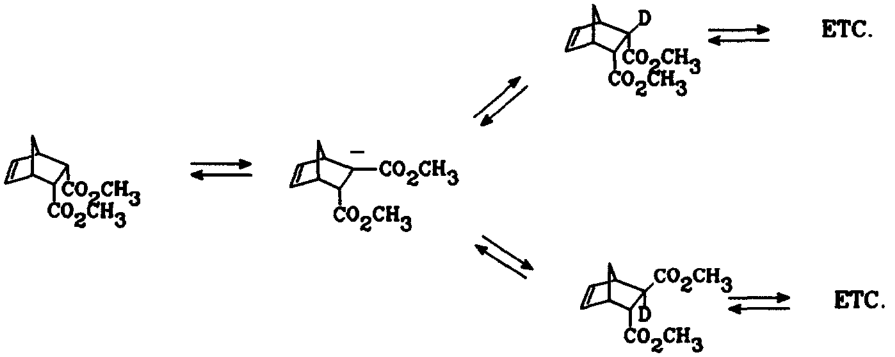
Although the enolate mechanism did not operate when N and X were exposed to activated alumina, this mechanism could account for the interconversion of the three diesters. One experiment reveals that this is the case. When a 3:1 mixture of diendo and diexo adducts was reacted with 700°-D/Al_2O_3 for 20 hours at room temperature, not only the recovered mixture of the three adduct diesters but also DMM and DMF (formed in the retro-Diels-Alder reactions) were extensively deuterated, and to approximately the same extent (Table 6). Careful analysis of the mass spectra of the adduct diesters revealed that deuterium exchange occurred exclusively at the positions α to the carbonyl groups.

It is reasonable to conclude that, because all of the compounds were deuterated to the same extent, the deuterium exchange reactions occur more rapidly than the retro-Diels-Alder reactions. Had the opposite been true, the adducts would have been more extensively deuterated than DMM and DMF.

Table 6. Deuterium Exchange of Diendo-Diexo Diesters (3:1) on 700°-D/Al_2O_3.

	Deuterum Distribution (%)		
Products (% Yield)	**d_0**	**d_1**	**d_2**
Recovered Diesters[a] (92)	11.8	34.5	53.8
DMM (6.4)	8.3	35.7	56.0
DMF (1.6)	12.2	36.2	51.5

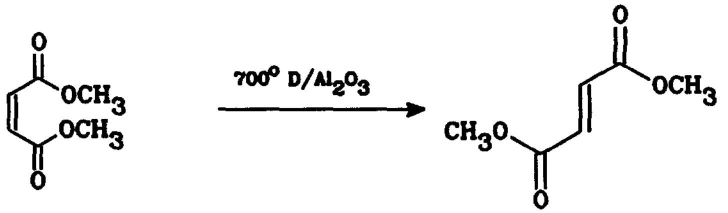
[a] The three esters were analyzed as a mixture.



(11)

Surprisingly another reaction is involved in the interconversion of the three Diels-Alder adducts. When DMM was treated with 700°-Al_2O_3 for 20 hours at room temperature, DMF was produced in 27.7% yield. DMM did not isomerize to DMF on 400°-Al_2O_3. DMF, on the other hand, did not yield DMM under either set of conditions. Interestingly, isomerization on 700°-D/Al_2O_3 did not result in any deuterium incorporation on DMF (eq. 12). This acid-catalyzed reaction is extraordinary because the isomerization does not occur when DMM is treated with the powerful Lewis acid $AlCl_3$ in CH_2Cl_2. One can conclude that DMM reacts with a surface site to form a complex with a considerably weakened carbon-carbon double bond, thus permitting cis-trans isomerization to form the DMF-surface complex. Regardless of the mechanistic details, this isomerization has synthetic potential.

(12)



Although it is probably not possible to ascertain all the details of how the three diesters interconvert, a careful analysis of the data obtained on 700°-Al_2O_3 did reveal that, of the three competing processes, the enolate chemistry occurs most rapidly and the cis-trans isomerization of DMM to DMF is slowest, with the retro-Diels-Alder reaction occurring at an intermediate rate. Furthermore, by observing these interconversions on increasingly more activated alumina, it is clear that the three reactions come into prominence in the same order.

Why is the enolate chemistry dominant for the CP-DMM and CP-DMF adducts but is not operational for the CP-MA adducts, N and X? The issue revolves around the relative acidities of the Diels-Alder adducts and the surface OH groups. OH^- is calculated to have a pK_a of 36 or greater in aqueous solution.[31] O^{-2} is basic enough to abstract a proton α to the carbonyl group of a monoester, which has a pK_a of 24.5,[32] in aqueous medium. On the solid, the basicity of O^{-2} is moderated by its close proximity to surrounding Al^{+3} cations such that the pK_a of surface OH^- is presumably less than 24.5. We have demonstrated that activated D/Al_2O_3 is basic enough to deuterate CP, which has a pK_a of 15,[33] ketones[24] with pK_a's around 20,[32,34] and phenylacetylene[24] with a pK_a of 18.5.[34] Thus, surface OH^- must have a $pK_a \geq 20$. For the CP-DMM and CP-DMF adducts, the second ester group at a position β to the first must be sufficiently electron withdrawing to decrease the pK_a from the value of 24.5 observed for the monoester adducts to a value closer to or even less than the pK_a of surface OH^-.

Experimental Section:

General.

All chemicals used in this study were reagent grade and purchased from commercial sources. The alumina was Brockmann Activity 1 neutral alumina purchased from Aldrich Chemical Company. ^1H and ^{13}C

NMR spectra were recorded on Jeol FX 90Q and Brucker AC-250 spectrometers. Preparative gas chromatography (GC) was performed on a Varian Aerograph Series 1700 instrument, analytical GC on Varian Model 3700 and Hewlett-Packard HP 5890 instruments, and GC/MS on a Hewlett-Packard HP 98785A instrument. Alumina was activated[24] and deuterated alumina (D-Al_2O_3) prepared[24] by literature procedures. 700°- and 800°-Al_2O_3 were prepared in quartz vessels. The deuterium content of the solid was determined by literature methods[24] and all D-Al_2O_3 contained a mole fraction of $\geq$ 0.95 D. The deuterium content of a molecule was determined by mass spectrometry from the intensity of the compound's parent ions taking into account the contributions from ^{13}C which can be obtained from mass and abundance tables.[35]

Reaction of Cyclopentadiene with Methyl Acrylate.

The following procedure is representive. To a 50-mL round-bottomed flask fitted with a condenser and stirring bar was added, under an inert gas (N_2 or Ar), freshly prepared cyclopentadiene (7.50 mmol, 0.495 g), methyl acrylate (7.50 mmol, 0.645 g), and 10 grams of unactivated alumina. The reaction was maintained at 50° (oil bath) for 5 h with stirring. After cooling, the unreacted starting materials and products were removed from the solid by extraction with anhydrous ether. After the ether was removed in vacuo, the yields of products were determined by GC (peak areas were calibrated with a known amount of an internal standard). The ratio of diastereomers was determined by GC and by integration of the methoxyl resonances in the ^1H NMR spectrum. Care was taken to insure that the retro-Diels-Alder reaction did not occur during GC analysis. Compounds were isolated by preparative GC and characterized by standard spectroscopic methods.

Epimerization of X to N.

The following is representive of the epimerization reactions run on alumina and deuterated alumina. In a 50-mL round-bottomed flask was placed, at 0°, 1.86 g of 400°-D/Al_2O_3 (96% D) and methyl 5-*exo*-2-norbornenecarboxylate (X) (1.00 mmol, 0.154 g) (isolated by prep GC on a 30% carbowax 20M on chromasorb W column). The slurry was allowed to stir at 60° for 24 h. After cooling, the solid was diluted with 10 mL of acetone. GC-MS revealed a 90:10 mixture of exo and endo esters, neither of which contained deuterium.

Isomerization of DMM to DMF on 700°-Al_2O_3.

To a 250 mL round-bottomed flask containing 25.0 g of alumina that had been activiated at 700° was added dropwise (via syringe), under an argon atmosphere, dimethyl maleate (1.25 mmol, 0.180 g). The reaction was stirred for 20 hours at ambient temperature. The solid was extracted into ether which was then removed in vacuo. The product mixture was analyzed by GC and GC/MS.

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