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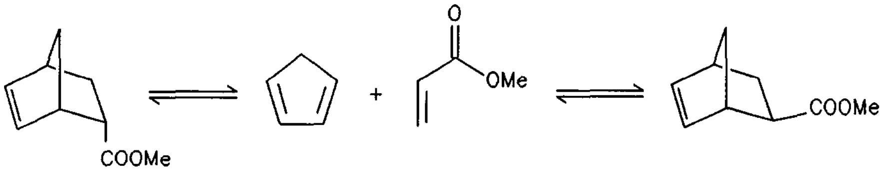
CYCLOADDITION REACTIONS OF DIMETHYL MALEATE AND FUMARATE WITH CYCLOPENTADIENE ON γ-ALUMINA. COMPETING MECHANISMS FOR EPIMERIZATION OF THE DIELS-ALDER ADDUCTS.

Satinder Bains, Richard M. Pagni* and George W. Kabalka*

Department of Chemistry, University of Tennessee,
Knoxville, Tennessee 37996-1600 USA

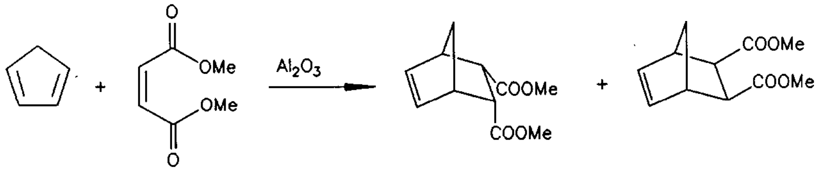
Summary: The Diels-Alder adducts, formed in the reaction of cylcopentadiene and dimethyl maleate and fumarate, epimerize on γ-alumina by competing mechanisms involving the retro-Diels-Alder reaction and enolates.

Previous work has shown that the diastereoselectivities observed in the Diels-Alder reactions of cyclopentadiene (CP) with methyl acrylate (MA) and optically active menthyl acrylate on the surface of γ-alumina are profoundly influenced by the activity of the solid.[1,2] Selectivities obtained on alumina activated by heating at 400° under vacuum, for example, are comparable to those observed in solution.[3] In addition, the adducts epimerize on the activated alumina. In the case of the adducts formed in the reaction of CP and MA, the epimerization occurs through a retro-Diels-Alder reaction, slowly on the 400°-solid and much more rapidly on 800°-solid.[1] We wish to report at this time that the dramatic increases in diastereoselectivity observed in the cited examples above also occur when CP is treated with dimethyl maleate (DMM) on alumina and that the resulting adducts, as well as the one formed in the reaction of CP with dimethyl fumarate (DMF), epimerize by competing pathways.



(1)

Treatment of CP with DMM on unactivated Brockmann alumina yielded the endo and exo Diels-Alder adducts in a 4.2:1 ratio. As shown in Table I, this ratio increased when the reaction was performed on increasingly more activated alumina, but not to the same extent as observed in the CP/MA reaction. The highest selectivity observed in the CP/DMM reaction, 15.6 on alumina activated at 700°, is a minimum value because, as described below, the adducts epimerize. It is worth noting that when the reaction was run in CH_2Cl_2 at room temperature in the presence of $AlCl_3$ a 20:1 ratio of the endo and exo products was produced.



(2)

Table I. Ratio of Products in the Reaction of Cyclopentadiene and Dimethyl Maleate.

REACTION CONDITIONS	ENDO : EXO	
	CP + MA[a,b,c]	CP + DMM[b,d]
Solution	3	3
Solution + $AlCl_3$		20
Alumina, Unactivated	5.8	4.2
Alumina, Activated at 200°	7.0	5.0
Alumina, Activated at 300°	10.3	
Alumina, Activated at 400°	51.9	7.0
Alumina, Activated at 700°		15.6

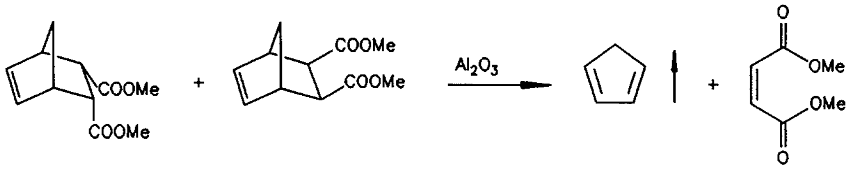
a) Reference 1. See also Parlar, H.; Baumann, R. *Angew. Chem. Int. Ed. Eng.* **1981**, *20*, 1014. b) One mmol of reagents (1:1) on 10 g of alumina. c) Run at 65°. d) Run at 20°.

The exo and endo adducts described above and the adduct obtained in the reaction of CP with DMF epimerize on alumina. Typical results, acquired by treating the esters with alumina activated at 700° for 20 hours at room temperature, are presented in Table II. Each adduct yielded the other two under these conditions, with the order of reactivity being: endo > exo > fumarate.

Table II. Epirimerization of Diels-Alder Adducts on 700°-Alumina at 55°

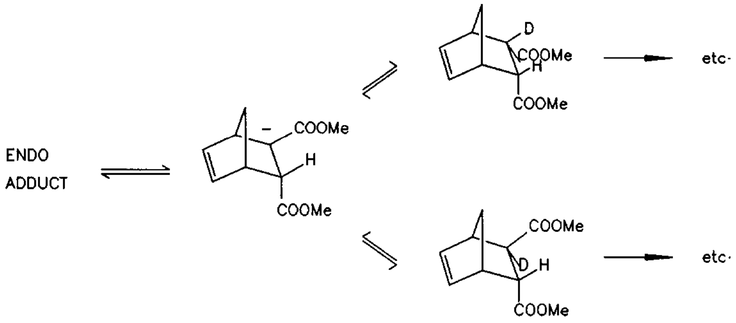
REACTANT	PRODUCTS (%)		
	ENDO	EXO	FUMARATE
Endo Adduct	59.1	13.3	27.6
Exo Adduct	6.4	84.1	9.5
Fumerate Adduct	1.6	2.3	95.6

The epimerizations occur by competing pathways which involve three distinct reaction types. Because the CP/MA Diels-Alder products epimerize by the retro-Diels-Alder mechanism[1], this mode of epimerization was studied first. When a 3:1 admixture of endo and exo adducts was subjected to 700°-alumina at 55° for 20 hours in the presence of the dienophiles MA, benzoquinone and tetracyanoethylene, no CP adducts which incorporated the dienophiles were formed. Nonetheless, the retro-Diels-Alder mechanism does occur. When the adducts were subjected to alumina under conditions where the volatile CP can escape from the surface, DMM is formed.



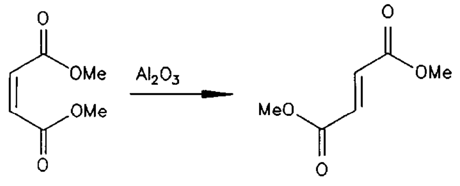
(3)

When the admixture of endo and exo norbornenes were subjected to deuterated alumina,[4] activated at 700°, at room temperature for 20 hours, the recovered endo and exo adducts, the epimerized fumarate adduct, and DMM and DMF, formed in the retro-Diels-Alder reaction of the above three norbornenes, were all extensively deuterated.[5] Careful analysis of the mass spectra of the norbornenes showed that they were deuterated exclusively at the two methine positions adjacent to the carbomethoxyl groups. These exchange reactions clearly occur through enolate chemistry.



(4)

A third reaction contributes to the epimerization chemistry. When DMM was treated with 700°-alumina at room temperature for 20 hours, a 27.7% yield of DMF was produced.[6] This isomerization does not occur on 400°-alumina. DMF, on the other hand, did not yield any measurable amount of DMM under the same conditions. The 700°-alumina is an extraordinary Lewis acid because DMM does not yield DMF when treated with the powerful Lewis acid $AlCl_3$ in CH_2Cl_2.[7] Because of the isomerization of DMM to DMF, it is possible to convert the endo (and exo) adducts into the fumarate adducts via the retro-Diels-Alder reaction.



(5)

Because of the complexity of the epimerization chemistry, it is probably not possible to unravel all its details, but the following statements are valid: (1) On 700°-alumina, the relative rates of the contributing reactions are: enolate > retro-Diels-Alder > DMM/DMF isomerization, (2) On increasingly more active alumina, the reactions are initiated in the same order.

It is not surprising that the retro-Diels-Alder chemistry is observed here because it was also observed for the CP/MA adducts as well.[1] What is surprising is that the enolate chemistry is prominent in the present examples but does not occur for the CP/MA adducts. The presence of a second electron withdrawing carbomethoxy group must be sufficient to make the methine hydrogens acidic enough to undergo exchange. These results also illustrate that activated Al_2O_3 is simultaneously a strong acid and a strong base. Such behavior is not possible in solution.[8]

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3. (a) Farmer, R. F.; Hamer, J. *J. Org. Chem.* **1968**, *31*, 2418. (b) Oppolzer, W.; Kurth, M.; Reichlin, D.; Moffat, F. *Tetrahedron Lett.* **1981**, 2545 (c) Isaacs, N. S. *Physical Organic Chemistry*, Longman Group/Wiley, 1987; pp. 704-706.
4. Gaetano, K.; Pagni, R. M.; Kabalka, G. W.; Bridwell, P.; Walsh, E.; Underwood, M. *J. Org. Chem.* **1985**, *50*, 499.
5. The recovered Diels-Alder adducts were analyzed as a mixture 53.8% d_2, 34.5% d_1, and 11.8% d_0. DMM yielded 56.0% d_2, 35.7% d_1, and 8.3% d_0. DMF yielded 51.5% d_2, 36.2% d_1, and 12.2% d_0.
6. When this reaction was carried out on deuterated alumina, there was no incorporation of deuterium into the esters.
7. Al_2O_3 is at best a weak Brønsted acid.
8. For other examples of Diels-Alder reactions occuring on alumina see: (a) Parlar, H.; Baumann, R. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 1014. (b) Koreeda, M.; Ricca, D. J.; Luengo, J. I. *J. Org. Chem.*, **1988**, *53*, 5586.

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