Catalytic Effect on the Mechanism of [2 + 2] Polar Cycloadditions

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The Lewis acid-catalysed reaction between hydroxyethylene and acrylaldehyde has been studied by the MINDO/3 method. The potential barriers for the uncatalysed and catalysed reactions are determined by the second and first transition states respectively. The main effect of the catalyst is to advance the first transition state along the reaction co-ordinate and to increase the zwitterionic character of the intermediate. An insight into the catalytic action is obtained.

The catalytic effect of Lewis acids on several cycloadditions has been known for a long time.[1,2] An increase in the rate of [2 + 2] cycloadditions brought about by $AlCl_3$ has recently been reported.[3-8] It is generally admitted that the catalytic action is due to complex formation between the Lewis acid and the electron-deficient alkene.[7]

Cycloaddition reactions can be classified as ionic or non-ionic, depending on whether charge transfer and fundamental configurations cross or do not cross along the reaction path. Acid catalysis of cycloaddition reactions has been interpreted by Epiotis [9,10] in terms of the stabilization produced by Lewis acids on the charge transfer configuration. In non-ionic reactions, there is a greater mixing of fundamental and charge transfer configurations in the catalysed reactions than in the uncatalysed ones. This causes a lowering of potential barriers, without substantially changing the positions of transition states along the reaction co-ordinate. In contrast, in ionic reactions, the stabilization of the charge transfer configuration in the catalysed reaction makes the transition state occur earlier on the reaction co-ordinate, which implies a barrier lowering.

In non-ionic reactions, it is sufficient to introduce the effect of the catalyst on reactants and transition states of the uncatalysed reaction, but in the ionic reactions it is necessary to locate the transition states in a more complete potential hypersurface including catalyst.

Huisgen [11,12] has suggested that [2 + 2] polar cycloadditions take place *via* a zwitterionic intermediate; thus they belong clearly to the class of ionic reactions. It is therefore of great interest to study the effect of a catalyst on such reactions, since, as mentioned before, the catalyst modifies the position of transition states in the potential hypersurface.

We have previously studied the gas-phase [2 + 2] polar cycloadditions between hydroxyethylene and 1,1-dicyanoethylene,[13] and between hydroxyethylene and acrylaldehyde,[14] where the hydroxy group has been taken as a model for the alkoxy group. In both reactions, the path leading to 1,2-disubstituted cyclobutanes is more favourable than that leading to 1,3-disubstituted cyclobutanes. Both reactions proceed through a two-step mechanism, having the greatest energy maximum at the second transition state. The intermediate presents little zwitterionic character, in contrast to Huisgen's [11,12] claim. On the other hand, the second transition state exhibits greater charge transfer between the substituted ethylenes.

We now report a theoretical study of the effect of acids on the mechanism of the reaction between hydroxyethylene and acrylaldehyde as an example of a [2 + 2] polar cycloaddition. We use as acids BF_3, NH_4^+, and H^+ as a limiting example. By studying the complete potential hypersurface, we have clarified the change in mechanism in going from the uncatalysed to the catalysed reaction, and on the other hand the changes in the catalyst itself and in the bonding between the catalyst and the substrate.

Table 1. Potential barriers (kJ mol^{-1}), lengths of bonds being formed, and charge transfers between hydroxyethylene and acrylaldehyde–boron trifluoride (distances in Å); charge transfer is given as fractional electron charge

	Catalyst	Energy	R_1	R_2	Charge transfer
First transition state	Uncat.	102.38	1.88	3.47	0.17
	BF_3	88.66	2.03	3.50	0.15
	NH_4^+	56.86	2.21	3.73	0.14
	H^+	33.68	2.39	3.82	0.13
Intermediate	Uncat.	98.70	1.67	3.63	0.34
	BF_3	59.91	1.59	3.28	0.54
	NH_4^+	−81.92	1.53	3.41	0.78
	H^+	−131.71	1.54	3.38	0.77
Second transition state	Uncat.	141.92	1.55	2.69	0.60
	BF_3	82.09	1.55	2.69	0.68
	NH_4^+	1.63	1.52	2.29	0.69
	H^+	−75.14	1.52	2.17	0.68
Product	Uncat.	−123.80	1.52	1.57	0.09
	BF_3	−130.62	1.52	1.58	0.14
	NH_4^+	−129.79	1.52	1.59	0.22
	H^+	−138.74	1.52	1.62	0.33

Calculation

Given that the uncatalysed reaction has a two-step mechanism, a good strategy to begin the study of the catalysed potential hypersurface is the direct localization of the reaction intermediate. To do this, we start from the intermediate found for the uncatalysed reaction,[14] just adding the catalyst to the acrylaldehyde fragment. Full optimization should then lead to the desired intermediate. From it, by means of the reaction co-ordinate method, using as independent variables each of the two lengths of new bonds being formed, two maxima may be found, one going from the intermediate to the reactants and another going from the intermediate to the products. These maxima can be used as good starting points for locating directly both transition states by McIver and Komornicki's method [15] (minimizing the root mean square gradient). By examining the eigenvalues of the force constant matrix, one can infer whether it is a transition state or another stationary point. Transition states are characterised by the existence of one and only one negative eigenvalue.

Since the MINDO/3 [16] method of energy calculation was used for the uncatalysed reaction, the present study was carried out by the same method. The GEOMO [17] program of Rinaldi was used for structure optimizations. McIver and Komornicki's method [15] of directly locating stationary points was implemented by the SIGMA and FORCE programs.

Results and Discussion

In Table 1 we present the results obtained for the reaction between hydroxyethylene and acrylaldehyde, leading to *trans*-2-hydroxycyclobutane-1-carbaldehyde. This reaction has been found to be more favoured than those leading to other possible adducts.

In the first column, the energies of the first transition state, intermediate, second transition state, and products for the uncatalysed and catalysed reactions are presented. Energies are always referred to reactants. In the remaining columns, the lengths of the two new bonds being formed and the charge transfer between the two fragments are shown. For both transition states and the intermediate, stabilization occurs in passing from the uncatalysed reaction to the catalysed one, but the degree of stabilization and the reasons for it are quite different.

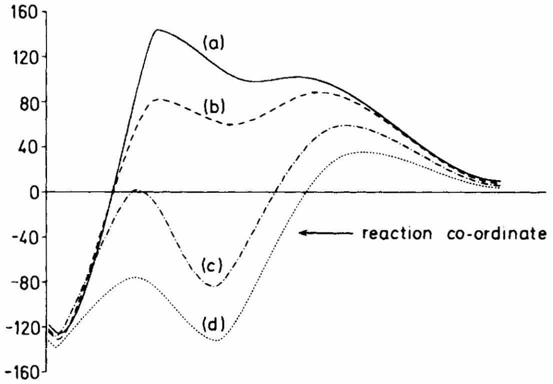

Figure 1. Energy profiles along the reaction co-ordinate for the reaction between hydroxyethylene and acrylaldehyde. Energies are referred to reactants: (a) uncatalysed reaction; (b) catalysed by BF_3; (c) catalysed by NH_4^+; (d) catalysed by H^+

For the first transition state, there is a small stabilization, which is not due to a charge transfer increase, but to an advance in the reaction co-ordinate. This can be observed in the variation of R_1 and R_2 with regard to different catalysts. This idea corresponds to that of Epiotis [10] in which for ionic reactions the stabilization of the charge transfer configuration advances the transition state on the reaction co-ordinate.

Energy stabilization by the catalyst is very strong in the intermediate. This is accompanied by a great increase in charge transfer. For the reactions catalysed by NH_4^+ and H^+ the intermediate clearly has zwitterionic character. From the changes in R_1 and R_2 in the catalysed reaction, one can see that the intermediate moves slightly backwards on the reaction co-ordinate.

The second transition state exhibits a stabilization parallel to that of the intermediate but a little smaller. The variation in charge transfer is also smaller than that of the intermediate, so for NH_4^+- and H^+-catalysed reactions the charge transfer is greater at the intermediate than at the second transition state. With respect to the reaction co-ordinate, the second transition state exhibits little variation.

Figure 1 shows the energy profiles along the reaction co-ordinate. In it, the profile variation with catalyst can be seen. For the uncatalysed reaction, the second transition state determines the potential barrier. As the catalyst strength increases, the first transition state determines the reaction

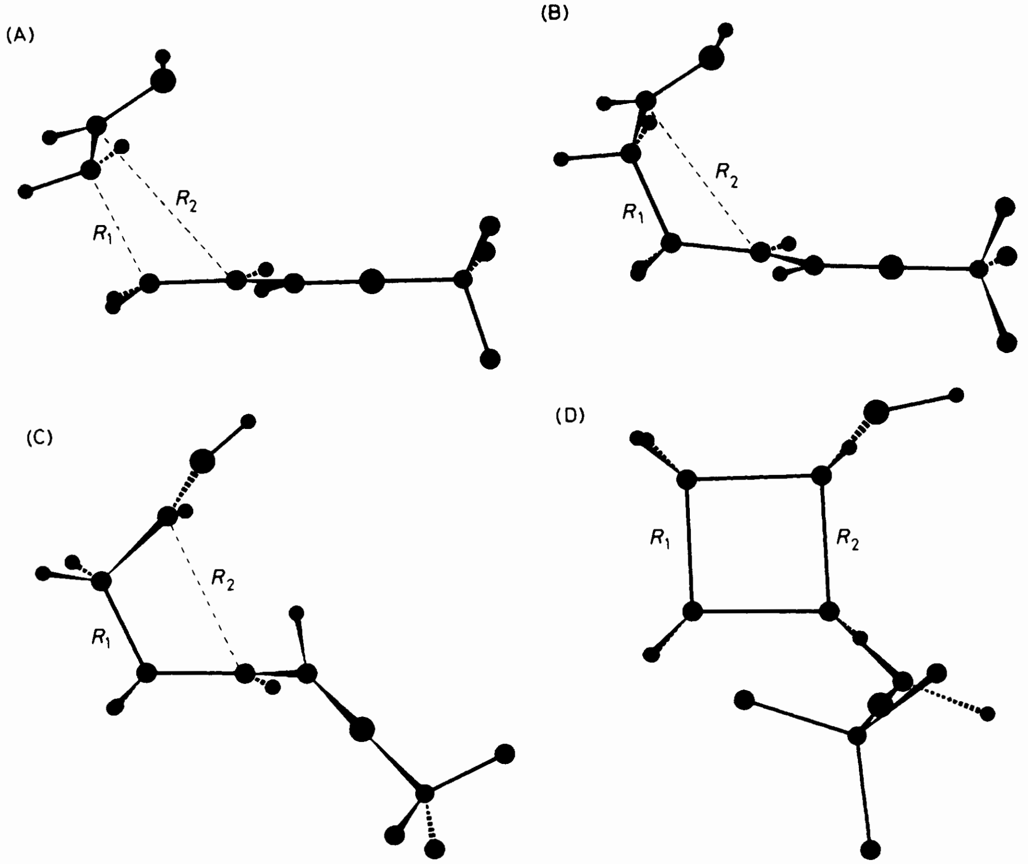

Figure 2. Structures for the BF_3-catalysed reaction between hydroxyethylene and acrylaldehyde: (A) first transition state; (B) intermediate; (C) second transition state; (D) product

Table 2. Charge transfer to BF_3, substrate–catalyst distance (Å) and Wiberg index, and OBF angle

Parameter	Reactants	1st T.S.	Intermediate	2nd T.S.	Product
$Q(BF_3)$	0.16	0.18	0.23	0.24	0.16
R(B–O)	1.45	1.43	1.40	1.40	1.45
W(B–O)	0.32	0.35	0.41	0.43	0.33
$<$(OBF)	106	107	109	109	105

Table 3. Charge transfer to NH_4^+, substrate–catalyst distance (Å) and Wiberg index, and H–N distance and Wiberg index

Parameter	Reactants	1st T.S.	Intermediate	2nd T.S.	Product
$Q(NH_4^+)$	0.24	0.34	0.73	0.51	0.26
R(H–O)	1.20	1.14	0.95	1.03	1.19
W(H–O)	0.31	0.42	0.90	0.63	0.33
R(H–N)	1.16	1.22		1.41	1.17
W(H–N)	0.60	0.58		0.48	0.26

potential barrier, and the process becomes clearly a two-step reaction. As has already been said, the decrease in the potential barrier of the first transition state is due to an advance on the reaction co-ordinate. The variations of the intermediate and second transition state along the reaction co-ordinate are not very great. There is a considerable increase of zwitterionic character of the intermediate, which makes the energy well deeper as the catalyst strength increases.

In Figure 2 the structures of the first transition state, intermediate, second transition state, and product for the BF_3-catalysed reaction are shown. The evolution of the two new bonds, already presented in Table 1, can be observed along with the variation of the geometric parameters of the remainder of the molecule. The changes in the bonding between the catalyst and acrylaldehyde, and in the catalyst itself, are worth noting.

Providing insight into the catalytic action, Table 2 shows, for the BF_3-catalysed reaction, the charge transfer to the catalyst, the distance and Wiberg index between it and the carbonyl oxygen, and the OBF angle. The charge transfer to the catalyst increases slightly in the intermediate and in both transition states, having its maximum at the second transition state, where the charge transfer from the hydroxyethylene to the acrylaldehyde is greatest. The catalyst acts by amplifying this charge transfer between the two fragments. This action implies that the strength of the bond between catalyst and substrate increases when going from reactants to the second transition state. In fact this can be seen in the same Table by looking at the B–O bond length change, or the B–O Wiberg index variation. When the strength of the catalyst–substrate bond increases, the hybridization of the boron atom becomes more clearly tetrahedral. All the changes in the substrate–catalyst bond and the catalyst itself show neatly that the geometric parameters of the catalyst are actually included in the reaction co-ordinate. Bonding between catalyst and substrate is looser in reactants and products than in transition states and intermediate, which well describes the role played by a catalyst in a chemical reaction.

The changes in catalyst–substrate bonding and in the catalyst itself are increased in the NH_4^+-catalysed reaction, as shown in Table 3. First, the charge transfer to the catalyst is greater than in the preceding case. It reaches its maximum at the intermediate, parallel to the charge transfer between the two fragments. Secondly, the difference in bonding between the hydrogen and the oxygen and nitrogen atoms along the reaction co-ordinate is noticeable. In reactants and products, there is strong hydrogen bonding between NH_4^+ and acrylaldehyde, even though the hydrogen belongs to ammonia. In contrast, in both transition states, even though the hydrogen bonding is maintained, the hydrogen is transferred to acrylaldehyde. This reaches its maximum degree in the intermediate, where hydrogen bonding is broken and the hydrogen is bonded to the oxygen in the same manner as it is in the H^+-catalysed reaction. In this case the specific action of the catalyst is to transfer a proton to the acrylaldehyde fragment in transition states and the intermediate, whereas in reactants and products it is not transferred.

Conclusions

This study of the catalyst effect on [2 + 2] polar cycloadditions shows that the catalyst intervenes on the reaction co-ordinate. Bonding between substrate and catalyst is stronger at the intermediate phase of the reaction, owing to amplification of the charge transfer between the fragments by the catalyst. The main consequence of the intervention of the catalyst on the reaction co-ordinate is that the reaction mechanism changes dramatically in the catalysed reactions. This change is small with true Lewis acids such as BF_3, but is very strong with a specific acid catalyst like NH_4^+ or H^+. The fundamental change in [2 + 2] polar cycloadditions brought about by the catalyst is that the first transition state determines the potential barrier of the reaction, since there is a greater stabilization in both the intermediate and the second transition state. A noticeable increase in reaction rate is produced, although the lowering of the potential barrier at the first transition state is small. The most important facts are, on the one hand, the advance of the first transition state, and on the other the increase in zwitterionic character in the intermediate. These calculations are likely to be valid in the gas phase. From the charge transfer in the intermediate and the two transition states one can predict that the effect of a polar solvent will be a stabilization and an increase in zwitterionic character of the intermediate. Also, the potential barrier of the second transition state will be lowered.

In view of the present results it seems that, in a study of the catalytic effect in any reaction, the catalyst should not be introduced directly at the stationary points of the reaction; a new localization of stationary points on the complete potential hypersurface must be made.

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