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Adicity Dependence of Acid-Catalyzed Reactions and Changing Mechanism in Moderately Concentrated Sulfuric Acid[1,2]

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The acid-catalyzed isomerization of cis-2-methoxychalcone shows a complex rate profile when plotted against the acidity function in the region of 2–10 M sulfuric acid. This rate profile is shown to be the result of the superposition of the two mechanisms already established for the isomerization of substituted chalcones. At low acidities, the dominant reaction pathway is that involving the addition of water to the conjugate acid of the chalcone. At high acidities, as the activity of water is reduced, this mechanism is superceded by the unimolecular isomerization of the conjugate acid.

Introduction

The initial finding that there are two mechanisms readily accessible for the isomerization of appropriately substituted cis-chalcones[4,5] has been followed by studies detailing the corollaries of these two mechanisms as exemplified by judiciously chosen examples.[6] cis-Chalcone and negatively substituted cis-chalcone normally isomerize by a mechanism involving the slow addition of water at the β-carbon to give the enol of the β-hydroxy ketone. By working in 90% sulfuric acid, it was possible to slow sufficiently this reaction pathway so that the alternate carbonium ion mechanism (involving the direct unimolecular rotation of the conjugate acid of the chalcone), mechanism B, became predominant for all chalcones except cis-4-nitrochalcone. In the case of cis-4-methoxychalcone and for polymethoxychalcones, the carbonium ion mechanism was observed at all acidities at which the rate of isomerization is of reasonable magnitude.

The facts leading to the above conclusions are largely independent of the detailed form of the acidity dependence of the cis to trans isomerizations. Though there is a clear difference between the rate–H_0 profiles for mechanism A and mechanism B, sufficient evidence has been presented to establish these mechanisms without direct recourse to a detailed consideration of the shape of the rate–H_0 profile. In other words, these mechanisms have been established without recourse to the Zucker–Hammett hypothesis.[7,8] The original Zucker–Hammett hypothesis has undergone considerable modification in recent years. We have shown that rate-determining proton-transfer mechanisms may show unit slope correlation with H_0, rather than with molar concentration, exemplified in the cis to trans isomerization of cinnamic acids.[9] Kuivila and Nahabedian have shown that the protodeboronation of areneboronic acids[10] likewise involves rate-determining proton transfer and a good correlation of rate with H_0. Similarly the aromatic hydrogen exchange reactions[11,12] show correlation with the acidity function.

Recently, several modifications of the Zucker–Hammett hypothesis have been suggested in order to provide a more detailed classification of reaction mechanisms and acidity dependence. Taft[13] has pointed out that there is a close connection between the solvation of anilinium ions and carbonium ions and the acidity functions H_0 and H_R, and other facets of this question have been discussed by Bell,[14] suggesting that the role of water in any reaction should be expressed in terms of a net involvement of water, over and above that implicit in the acidity function H_0.

The suggestions of Bunnett[15] are much more explicit and detailed. He proposes that a distinction can be made among four types of mechanisms, distinguished by the "w" value, i.e., a function of the power to which the activity of water must be raised to provide satisfactory unit slope correlation between log k and H_0. Reactions involving nucleophilic reactions of water with organic cations are to be characterized by positive values of "w," and reactions involving a unimolecular reaction of the organic cation are characterized by negative values of "w."

With detailed knowledge regarding the mechanism of isomerization of a variety of substituted cis-chalcones in hand, we deemed it instructive to examine the isomerization of a suitable chalcone which would undergo a change in mechanism from the water addition mechanism to the unimolecular isomerization mechanism in the region of moderately concentrated sulfuric acid. The study of such a compound would provide a valuable experimental demonstration of the nature of reaction rate–acidity correlations in the region where a change in reaction mechanism occurs. It would serve to point out some of the potentialities and also possible pitfalls of these new interpretations. The restrictions imposed by chemical and physical reality are reasonably severe. The acidity region in which the two mechanisms are directly competitive should lie between 3 and 10 M sulfuric acid for a change in mechanism to show clearly. It would be advantageous for the pK of the organic substrate to lie well outside the range where mechanisms are competitive.

The previously reported results on cis-2-methylchalcone[6] show part of the picture; in moderately concentrated sulfuric acid, mechanism A is dominant; above the pK for cis-2-methylchalcone, mechanism B represents the pathway of isomerization. However, the complexities associated with the fact that the change in mechanism occurs at an acidity practically coincident with the pK made this particular compound less than ideal. Measurements on cis-4-methylchalcone show some evidence for a change in mechanism; however, this occurs just as the rate of reaction becomes intolerably fast.

The present report is largely concerned with cis-2-methoxychalcone, which represents a satisfactory example.

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(7) L. Zucker and L. P. Hammett, ibid., 61, 2791 (1939).

(8) F. A. Long and M. A. Paul, Chem. Rev., 57, 935 (1957).

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(11) F. A. Long and J. Schulze, ibid., 83, 3340 (1961).

(12) A. J. Kresge and Y. Chiang, ibid., 83, 2877 (1961).

(13) R. W. Taft, Jr., ibid., 82, 2965 (1960).

(14) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959.

(15) J. F. Bunnett, J. Am. Chem. Soc., 83, 4956, 4968, 4973, 4978 (1961).

Experimental

All compounds used have been characterized in our earlier reports.[6,16]

Kinetic methods have been described previously.[4,6]

Results

Rate of Isomerization of cis-4-Methylchalcone.—The observed rate of isomerization of cis-4-methylchalcone (Table I) shows the typical rate profile associated with mechanism A, in which the rate does not increase as rapidly as the acidity function would predict. A detailed examination of the data in the region of the highest acidity accessible suggests that in a solution of $H_0 = -4.80$, about 20–30% of the observed total rate is due to the incursion of the carbonium ion mechanism (mechanism B). This conclusion is based on the following. The ratio of observed rates[4] for the isomerization of cis-chalcone compared to cis-4-nitrochalcone remains sensibly constant at 7.5 throughout the region of 5 to 10 M sulfuric acid. The ratio of observed rates of cis-4-methylchalcone to cis-chalcone likewise remains sensibly constant from 3 M sulfuric acid to 7 M sulfuric acid at 1.9:1. However, from 7 to 9 M sulfuric acid the rate ratio rapidly rises with cis-4-methylchalcone isomerizing 3 times more rapidly in 9.28 M sulfuric acid.

TABLE I

RATE OF ISOMERIZATION OF cis-4-METHYLCHALCONE AT 25.00[a]

H₂SO₄, M	$k \times 10^4$, sec.⁻¹	H_0	$\log k + H_0$
2.55	0.379	−1.04	−5.46
4.29	1.63	−1.87	−5.66
5.90	5.50	−2.74	−6.00
6.25	7.70	−2.94	−6.05
6.65	11.1	−3.20	−6.16
7.14	17.8	−3.50	−6.25
7.90	30.1	−3.95	−6.47
8.69	53.3	−4.44	−6.71
9.28	82.1 ± 4[b]	−4.84	−6.93

[a] All reactions were carried out in 5% dioxane–95% aqueous acid, using kinetic method I and 10-cm. cells. [b] Average of 3 values.

At this highest acidity there is also evidence that an appreciable fraction of cis-4-methylchalcone is present as the salt,[16] as shown by the changes in the spectrum. This, of course, will make for a further correction and for a net increase in the fraction of cis-4-methylchalcone isomerizing by way of the carbonium ion mechanism.

The calculation of the rate of the unimolecular isomerization from the ρ–σ^+ correlation discussed previously[6] is consistent with the conclusion reached above that in 9.3 M sulfuric acid the isomerization of cis-4-methylchalcone is occurring in part by both mechanisms.

Rate of Isomerization of cis-2-Methoxychalcone.— The isomerization of cis-2-methoxychalcone takes place at moderate speeds in the region of 2 to 10 M sulfuric acid. This covers the region in which the acidity function H_0 deviates substantially from the molar concentration of sulfuric acid (at the low end of the above concentration range) up to the region in which 2-methoxychalcone is substantially protonated.

The rate data at 25° are presented in Table II. A fairly detailed discussion of these data is warranted. Starting at the highest acid concentration in which measurements were made, the slope of a log k vs. H_0 plot is 1.2. This is very similar to the slopes found for cis-4-methoxychalcone,[4] cis-2,4-dimethoxychalcone,[6] and cis-2,6-dimethoxychalcone.[6] It is also entirely consistent with the rate behavior of cis-2-methylchalcone in the 70–90% sulfuric acid region and of cis-chalcone itself in the 90–95% sulfuric acid region.[6] This, then, is

(16) D. S. Noyce and M. J. Jorgenson, J. Am. Chem. Soc., **84**, 4312 (1962).

the region in which the isomerization is taking place by mechanism B, the carbonium ion mechanism which we have described in detail earlier.[4]

TABLE II

RATE OF ISOMERIZATION OF cis-2-METHOXYCHALCONE IN 5% DIOXANE–95% AQUEOUS SULFURIC ACID

H₂SO₄, M	H_0	k, sec.⁻¹	$\log k + H_0$	Fraction isomerizing by mechanism B	$\log a_{H_2O}$
		$T = 25.00°$			
2.83[a,g]	−1.16	2.46 × 10⁻⁵	−5.77	<0.10	−0.08
3.56[a]	−1.51	4.28 × 10⁻⁵	−5.88		− .11
4.29[a]	−1.87	1.17 ± 0.01 × 10⁻⁴[d]	−5.80		− .16
4.83[b]	−2.12	1.89 × 10⁻⁴	−5.84	0.12	− .20
5.42[b]	−2.42	3.50 × 10⁻⁴	−5.88	.15	− .26
5.81[a,h]	−2.66	5.02 ± 0.11 × 10⁻⁴[d]	−5.96	.20	− .30
6.18[b]	−2.92	7.22 × 10⁻⁴	−6.06	.27	− .34
6.65[b]	−3.16	1.31 × 10⁻³	−6.04	.32	− .40
7.14[b]	−3.50	2.27 × 10⁻³	−6.14	.50	− .46
7.51[c]	−3.73	3.25 ± 0.07 × 10⁻³[e]	−6.22	.62	− .51
7.96[c]	−4.00	5.59 ± .24 × 10⁻³[e]	−6.25	.80	− .58
8.18[c]	−4.15	7.31 ± .46 × 10⁻³[f]	−6.29	.85	− .62
8.49[c]	−4.33	1.22 ± .065 × 10⁻²[e]	−6.24	.90	− .67
8.87[c,h]	−4.55	2.31 ± .15 × 10⁻²[e]	−6.19	> .90	− .73
		$T = 45.00°$			
1.00[b,g]	−0.20	3.04 × 10⁻⁵	−4.72		
2.83[b,g]	−1.16	1.86 × 10⁻⁴	−4.88		
3.56[a]	−1.51	3.61 × 10⁻⁴	−4.95		

[a] Method I, 10-cm. cells. [b] Method II, 10-cm. cells. [c] Method III. [d] Average of 2 values. [e] Average of 3 values. [f] Average of 5 values. [g] $E_a = 19.1$ kcal., $\Delta H^{\ddagger} = 18.5$ kcal., $\Delta S^{\ddagger} = -21.3$ e.u. [h] 14.7% of cis-2-methoxychalcone present as BH⁺. [i] Activity of water in aqueous sulfuric acid.

In contrast, the rate of isomerization in the lowest acid region—from 2 to 4 M sulfuric acid—shows a slope in a log k vs. H_0 plot of only 0.8. This slope, at these sulfuric acid concentrations, is typical of isomerization by the mechanism involving the slow, rate-determining attack of water upon the conjugate acid of the chalcone. Further, the activation parameters in this region support this mechanism.

Between these two extremes, the rate profile describes a gentle reverse "S-shaped" curve. This curve is shown in Fig. 1. The rate in the intermediate portion of the acid concentration range is then a composite rate for the two competing mechanisms.

The rate in this middle range of sulfuric acid concentration is very satisfactorily fitted by the composite of two curves, one typical of mechanism B and the other typical of mechanism A. These curves are sketched in Fig. 1.

Let us now examine the question of using the form of such an acidity dependence to suggest a mechanism for a reaction in a case where the mechanism was otherwise unknown. Were a limited amount of rate data obtained, and that over a restricted range of acidities, an observed slope could vary from 0.8 to 1.2, with only minor discrepancies from "linear" correlation. Though it is redundant to emphasize the value of a maximum range of acid concentrations in any H_0 studies, the present instance serves to emphasize forcefully the pitfalls of a narrow range of data.

A further way of examining the data is suggested by the work of Bunnett.[15] A plot of (log k + H_0) vs. log a_{H_2O} is constructed and the slope, "w," is used as a characteristic of the reaction under study. If, as suggested by Bunnett, "w" is a constant which characterizes the particular involvement of water, such a plot should reflect any changes in mechanism by showing a changing value of "w."

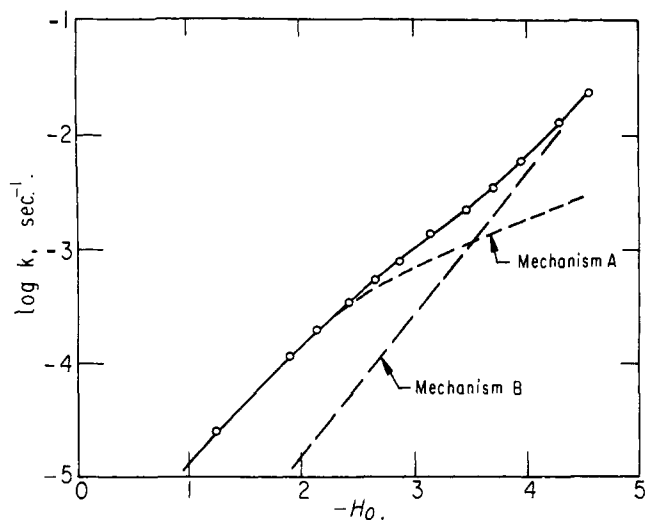It should be emphasized that constancy of the "w" is assumed in such an analysis, and that activity coeffi-

Fig. 1.—Rate of isomerization of cis-2-methoxychalcone.

cients are expected to remain constant throughout the acidity region used. A further requirement is that the compound in question behave as a Hammett base Neither of the latter can be assumed to be true *a priori*, and in this particular case evidence has been presented[6] that the activity coefficients do not remain constant. In Bunnett's analyses of available data, deviations from linear plots were often observed and the data leading to linear plots are generally obtained from rate data over a somewhat limited range of acid concentrations. We have examined the question of constancy of "*w*" values for the isomerization of chalcones shown to proceed by mechanism A, the water addition mechanism. In all cases, the rate data obtained cover a wide range of acidity and extend into the upper end of the "moderately concentrated acid" region; the test of Bunnett's analysis is, therefore, more severe. The plots constructed reveal in every case that "*w*" has a gradually decreasing value; for 4-nitrochalcone, the "*w*" is close to 3 in the 4–5 M acid region, but changes to about 1.2 at 10 M acid. Similar results were obtained for all of the other chalcones which isomerize by the same mechanism. For the isomerization of chalcones by mechanism A, "*w*" is not a constant.

Bunnett[17] has suggested that a changing "*w*" value may be used as a criterion for mixed mechanism, but has pointed out that the common result is that "*w*" will be of intermediate value. This is to be expected if the relative importance of two mechanisms remains constant with acidity. However, if two mechanisms differ in their acidity dependence, increase in acidity will affect the relative importance of the two mechanisms with the result that one mechanism eventually pre-

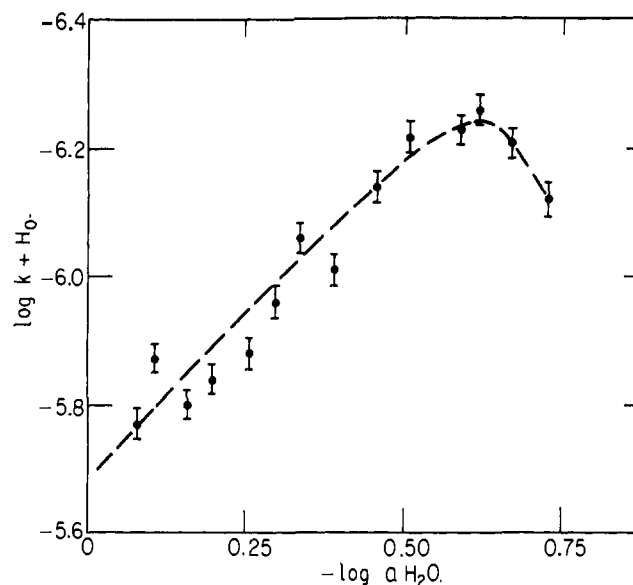(17) J. F. Bunnett, *J. Am. Chem. Soc.*; **83**, 4964 (1961).

Fig. 2.—Variation of (log k + H_0) for cis-2-methoxychalcone with activity of water.

dominates. In such a case, the resulting change in mechanism might be expected to be evident from a changing "*w*" value in a Bunnett plot. In the case of cis-4-methylchalcone the incipient change in mechanism at the highest acidity is not obvious from a Bunnett plot, partly because the slowly increasing "*w*" value due to incursion of mechanism B is offset by a slowly decreasing "*w*" value typical of mechanism A.

In the case of cis-2-methoxychalcone the change in mechanism is apparent from the observed changes in slope of a log k vs. H_0 plot (Fig. 2). Careful consideration of relative rates also supports this conclusion. The rate data for cis-2-methoxychalcone are particularly suited for further detailed analysis as they extend over a considerable region of water activity and the change from one mechanism to the other is almost complete. A Bunnett plot (Fig. 2) of the data is very instructive. In contrast to the very *slowly* decreasing "*w*" values observed with other chalcones, the Bunnett plot reveals a very *abrupt* change in "*w*" from a positive value to a negative value in the region in which mechanism B is becoming the predominant pathway. It is concluded that this novel application of a Bunnett analysis can be very useful in the detection and analysis of changes in mechanism.

A similar illustration of this application of "*w*" values has recently been made by Buchholz and Powell[18] in the analysis of rate data obtained from the decomposition of hyponitrous acid.

(18) J. R. Buchholz and R. E. Powell, *ibid.*, **85**, 509 (1963).