

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY 4, CALIF.]

## The Isomerization of Substituted *cis*-Chalcones in Sulfuric Acid. Consequences of the Two Mechanisms<sup>1,2</sup>

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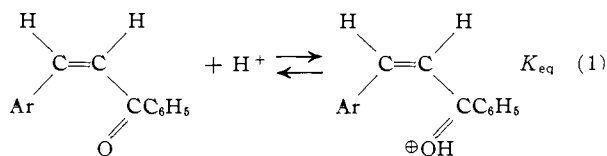
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The rate of the acid-catalyzed isomerization of *cis*-4-nitrochalcone reaches a maximum at 78% sulfuric acid, *i.e.*, at the *pK* for *cis*-4-nitrochalcone. At higher concentrations of sulfuric acid, the observed rate of isomerization decreases sharply, owing to the rapid decline in the activity of water. The behavior of *cis*-chalcone is similar, with the rate reaching a maximum at 72% sulfuric acid and then declining to 90% sulfuric acid. At the latter acid concentration a rate minimum is observed. In 96% sulfuric acid the mechanism of the isomerization of *cis*-chalcone has changed to the carbonium ion mechanism. Structural modifications of the chalcone structure have been studied in order to delineate further the conditions under which isomerization may change from mechanism A to mechanism B. Introduction of *o*-substituents results in a decrease in the observed rate of isomerization by mechanism A (the water addition mechanism) and therefore allows the incursion of isomerization by mechanism B (the carbonium ion mechanism) to be observed for a wider range of substituents. In the carbonium ion mechanism extreme sensitivity to the electron-donating ability of substituents is observed. *cis*-2,4,6-Trimethoxychalcone undergoes isomerization faster at pH 2 than *cis*-chalcone in 98% sulfuric acid. Comparison of the rates of isomerization for *cis*-chalcone, *cis*-4-methoxychalcone, and dimethoxychalcones and trimethoxychalcones reveals that the introduction of a *p*-methoxyl group accelerates the isomerization by way of the carbonium ion mechanism by a factor of  $10^4$  to  $10^5$ . Correlations of the rates for isomerization of *cis*-chalcones by mechanism B with  $\sigma^+$ -substituent constants gives a  $\rho$  of  $-7$ .

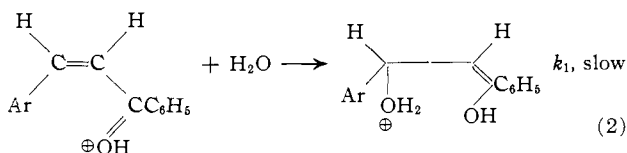
### Introduction

In previous papers<sup>4-6</sup> we have reported our studies of the *cis* to *trans* isomerization of chalcone and of several 4-substituted chalcones. These studies suggested that there are two mechanisms available for the *cis* to *trans* isomerization of  $\alpha,\beta$ -unsaturated ketones. Data were obtained from activation parameters, acidity dependence, relative rates, and kinetic solvent isotope effects to support and to delineate the two proposed mechanisms.

The first (and more generally applicable) mechanism, A, involves the nucleophilic addition of water to the  $\beta$ -carbon of the conjugate acid of the substituted *cis*-chalcone (eq. 2). It is to be noted that this is effectively a 1,4-addition process. This mechanism was observed to be operative with *cis*-chalcone (I) itself and with *cis*-4-nitrochalcone (IV) and *cis*-4-chlorochalcone (III) in moderately concentrated sulfuric acid.



I, Ar = C<sub>6</sub>H<sub>5</sub>-  
 III, Ar = *p*-ClC<sub>6</sub>H<sub>4</sub>-  
 IV, Ar = *p*-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>-



The alternative mechanism deduced, mechanism B, does not require the addition of water, but involves simply the slow unimolecular rotation about the C $_{\alpha}$ -C $_{\beta}$  bond in the conjugate acid (eq. 3) as the rate-determining process.

(1) For previous paper see Carbonyl Reactions. XI. D. S. Noyce and M. J. Jorgenson, *J. Am. Chem. Soc.*, **84**, 4312 (1962).

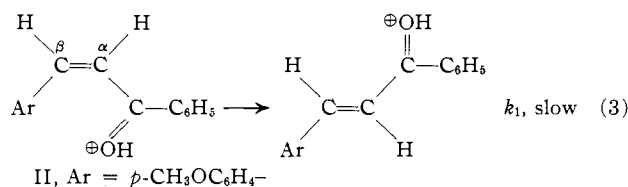
(2) Supported in part by grants from the National Science Foundation (G-13125) and the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of this fund.

(3) National Institutes of Health Postdoctoral Fellow, 1959-1961.

(4) D. S. Noyce, W. A. Pryor, and P. A. King, *J. Am. Chem. Soc.*, **81**, 5423 (1959).

(5) D. S. Noyce, G. L. Woo, and M. J. Jorgenson, *ibid.*, **83**, 1160 (1961).

(6) D. S. Noyce and M. J. Jorgenson, *ibid.*, **83**, 2525 (1961).

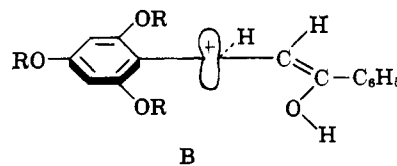


We shall call this mechanism the carbonium ion mechanism. It was found that *cis*-4-methoxychalcone (II) isomerizes by the carbonium ion mechanism.

Some consequences of these results are the subject of the present report. The first is: If the sulfuric acid concentration is sufficiently high that the substituted *cis*-chalcone is completely converted to its conjugate acid, further increase in the sulfuric acid concentration should cause the rate of isomerization to decrease in direct proportion to the decreasing activity of water.

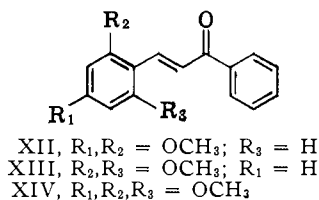
Secondly, it should be possible to find conditions under which the mechanism of isomerization will change from mechanism A to mechanism B. By reducing the activity of water the observed rate of isomerization by mechanism A may be reduced, and thus allow mechanism B to become competitive. Additionally, the introduction of *o*-substituents will provide some steric interference to the addition of water at the  $\beta$ -carbon, and likewise allow the carbonium ion mechanism to become competitive.

Thirdly, it is to be expected that the carbonium ion mechanism will show extreme sensitivity to the introduction of additional electron-donating substituents, as there is a full positive charge localized at the benzylic carbon in the transition state (B).



To examine the first of these consequences, we have studied the rate of isomerization of *cis*-4-nitrochalcone in more concentrated sulfuric acid than previously,<sup>6</sup> encompassing the range of 75-98% sulfuric acid. To seek information on the circumstances under which the change in mechanism may be observed, we have examined the isomerization of *cis*-chalcone in 75-95% sulfuric acid and the isomerization of typical *o*-substituted chalcones over a wide range of acid concentrations. Introduction of methoxy groups in the 2-, the

4-, and the 6- position will exert a very great influence on the stability of the proposed benzylic carbonium ion, suggested as the best representation for the transition state B of the latter mechanism of isomerization, and permit a more detailed study of the carbonium ion mechanism at lower acidities. Accordingly, we have prepared 2,4-dimethoxychalcone (XII), 2,6-dimethoxychalcone (XIII), and 2,4,6-trimethoxychalcone (XIV) and have studied the rate of isomerization of the corresponding *cis* isomers.



### Experimental

**Kinetic Methods.**—In addition to the methods previously described,<sup>6</sup> three additional procedures were used. Each of these methods was checked for consistency of the data with the other procedures and used as appropriate.

**Method I.**—The following procedure was particularly convenient for measuring the rate of isomerization under conditions where the half-life was only a few minutes. A solution of the *trans* isomer, in sulfuric acid of the desired concentration, was prepared as previously described. The solution, contained in a 10-cm. cell, was brought to thermal equilibrium (15 to 30 min.) in a thermostated cell compartment and block of the Beckman DU spectrophotometer and was irradiated with a General Electric 275-watt sun-lamp for periods of 10–60 sec. to establish the photodynamic *cis-trans* equilibrium, generally found to favor the *cis* isomer. During this irradiation period the cell was maintained in the thermostated cell block. Measurements of the rate of the acid-catalyzed conversion of the *cis* isomer were then carried out.

This method obviated the often cumbersome and tedious isolation and purification of the *cis* isomer.

**Method II.**—The position of the photodynamic equilibrium was found to be dependent on the acid concentration for various chalcones. For example, *trans*-4-nitrochalcone in concentrated sulfuric acid was not converted to a mixture rich in the *cis* isomer, but on the contrary, *cis*-4-nitrochalcone was very rapidly isomerized by visible light to the *trans* isomer in concentrated sulfuric acid.

This situation also points out an additional factor to which careful attention must be given in order to obtain meaningful results. In strongly acidic solutions in which 4-nitrochalcone is largely converted to its conjugate acid, the long wave length absorption band extends into the visible region of the spectrum for both the *cis* and *trans* salts. Under these conditions, a dilute solution (10<sup>-5</sup> to 10<sup>-6</sup> M) is rapidly equilibrated to the photodynamic equilibrium mixture by either daylight or room light. This phenomenon must be avoided in carrying out kinetic studies. It was necessary, therefore, to protect solutions of *cis*-4-nitrochalcone from visible light throughout the preparation and use of the solutions for kinetic runs. When the photochemical equilibrium in the acidic medium contained only small amounts of the *cis* isomer, the following method was employed. A 5-ml. dioxane aliquot of the *trans* isomer was irradiated in a 100-ml. volumetric flask to give an equilibrium mixture of the *cis* and *trans* isomers (generally 70–80% *cis* in neutral solvents). The solution for the kinetic runs was then made up to volume with sulfuric acid of the desired concentration, transferred to the Beckman cell, and after a brief period for temperature equilibration, readings were initiated. This method has the shortcoming that it is not suitable for kinetic runs in which the half-life is extremely short.

**Method III.**—This procedure was employed for very rapid isomerizations when method I did not yield a favorable *cis-trans* mixture on irradiation. It employed the *cis*-chalcone and was generally used at high acid concentrations where partial or complete conversion to the conjugate acid greatly facilitated dissolution of the chalcone.

The acid solution was brought to temperature equilibrium within the Beckman cell. Minute amounts of a concentrated solution of the *cis* isomer in dioxane were then introduced by means of a thin stirring rod, dipped into the cell with a few quick stirring movements. Readings were immediately initiated; if the rate of reaction permitted, a brief time interval was allowed for temperature equilibration before this. Duplicate runs were generally made; the reproducibility of the data by this procedure was somewhat less than with the other procedures. Even so, the average values obtained by this method agreed within 5% and are considered quite satisfactory considering the very short half-lives of the reactions followed in this fashion.

**Preparation of *cis*-2-Methylchalcone.**—A solution of 13.5 g. of *trans*-2-methylchalcone in 2 l. of benzene was irradiated with a 275-watt sun-lamp for a period of 3 days. The solvent was distilled and the residue treated with hexane. The insoluble material (*trans* isomer and polymeric material) was separated, and the hexane layer was concentrated to furnish additional amounts of insoluble material. The pale yellow hexane solution upon evaporation of the solvent afforded 9 g. of oil, whose infrared spectrum indicated that it consisted of essentially pure *cis*-2-methylchalcone. Fractional distillation afforded pure *cis*-2-methylchalcone, b.p. 140–142° (0.02 mm.); λ<sub>max</sub><sup>EtOH</sup> 255 mμ (ε 10,400), 240 mμ (ε 10,600), 300 mμ (ε 8900).

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>O: C, 86.45; H, 6.35. Found: C, 86.46; H, 6.28.

**2,6-Dimethoxychalcone (XIII).**—A solution of 8.3 g. of 2,6-dimethoxybenzaldehyde<sup>7</sup> and 6.0 g. of acetophenone in 50 ml. of ethanol and 25 ml. of 10% sodium hydroxide was stirred at room temperature for 12 hr., at which time the separation of a yellow oil was complete. Work-up by extraction afforded a yellow oil which was crystallized from methanol to give 10.0 g. (75%) of crystalline XIII. Three recrystallizations from methanol afforded flat yellow needles, m.p. 54–55°; λ<sub>max</sub><sup>EtOH</sup> 258 mμ (ε 7760), 340 mμ (ε 19,000).

*Anal.* Calcd. for C<sub>17</sub>H<sub>16</sub>O<sub>3</sub>: C, 76.10; H, 6.01. Found: C, 75.96; H, 5.83.

**Isomerization of *cis*-2,4,6-Trimethoxybenzylideneacetophenone in Sulfuric Acid-d<sub>2</sub>-Dioxane.**—A solution of 100 mg. of *trans*-2,4,6-trimethoxychalcone in 12 ml. of anhydrous dioxane in a 25-ml. volumetric flask was irradiated with a sun-lamp for 24 hr. The photodynamic equilibrium established contains about 80% of the *cis* isomer. The flask was made up to volume with 0.01 M (pH 1.64) sulfuric acid-d<sub>2</sub> and kept at 25° for 1 hr. After dilution with 20 ml. of deuterium oxide, crystals separated on cooling; total dry weight 70 mg. (70% recovery). The infrared spectrum (in CHCl<sub>3</sub>) was superimposable on that of the starting material, showing that no deuterium had been incorporated.

When *trans*-2,4,6-trimethoxychalcone was allowed to stand for a few minutes in a 30% aqueous (D<sub>2</sub>O)-dioxane solution 4.5 molar in sulfuric acid-d<sub>2</sub>, appreciable deuterium incorporation was observed. The recovered XIV, 60 mg. (60%) after recrystallization from methanol, m.p. 109–110°, showed an infrared spectrum differing markedly from either *trans*-2,4,6-trimethoxybenzylideneacetophenone-α-d<sub>1</sub> or authentic XIV. This is undoubtedly due to the introduction of deuterium into the 3- and 5-positions of the benzene ring.

**Preparation of *trans*-2,4,6-Trimethoxybenzylideneacetophenone-α-d<sub>1</sub>.**—A solution of 1.25 g. of acetophenone-α,α,α-d<sub>3</sub> and 2.06 g. of trimethoxybenzaldehyde in 5 ml. of dioxane was added to a solution of sodium deuteroxide, prepared by dissolving 0.3 g. (0.013 g.-atom) of sodium in 5 ml. of deuterium oxide. After 24 hr., a yellow oil separated, which crystallized on cooling to give 2.56 g. (86%) of 2,4,6-trimethoxybenzylideneacetophenone-α-d<sub>1</sub>, m.p. 108–109°. The infrared spectrum (in CHCl<sub>3</sub>) showed the presence of new bands at 1280, 1150, 1090, 950, and 290 cm.<sup>-1</sup>, and the absence of bands present in the undeuterated compound at 1140, 1030, 1010, and 980 cm.<sup>-1</sup>.

**Isomerization of *cis*-2,4-Dimethoxybenzylideneacetophenone in Sulfuric Acid-d<sub>2</sub>-Dioxane.**—A solution of 112 mg. of *trans*-2,4-dimethoxybenzalacetophenone in 12 ml. of dioxane in a 25-ml. volumetric flask was irradiated with a sun-lamp for 22 hr. The flask was made up to volume with 1.06 M sulfuric acid-d<sub>2</sub> and kept at 25° for 1 hr. Work-up by dilution with deuterium oxide and extraction with ether afforded 90 mg. of yellow oil, whose infrared spectrum was identical to that of the starting material. Chromatography on neutral Woelm III alumina gave an oil which could be crystallized from ethanol to give 30 mg. of crystalline XII.

**Other compounds** used have been described in previous papers.<sup>1,6</sup>

### Results

***cis*-4-Nitrochalcone (IV).**—The rate of isomerization of *cis*-4-nitrochalcone (Table I, Fig. 1) increases slowly as the sulfuric acid concentration is raised from 50 to 70%, reaching a maximum rate in 78% sulfuric acid.

In the acidity region of 70 to 80% sulfuric acid, the spectrum of IV likewise undergoes a pronounced change, associated with protonation of the carbonyl group and formation of the conjugate acid of IV.<sup>1</sup> As the rate of isomerization in this region has a half-life of at least 8 min., at 25° it is quite feasible to measure the basicity constant directly, in contrast to the other *cis*-chalcones which we have studied.<sup>1</sup> By lowering the

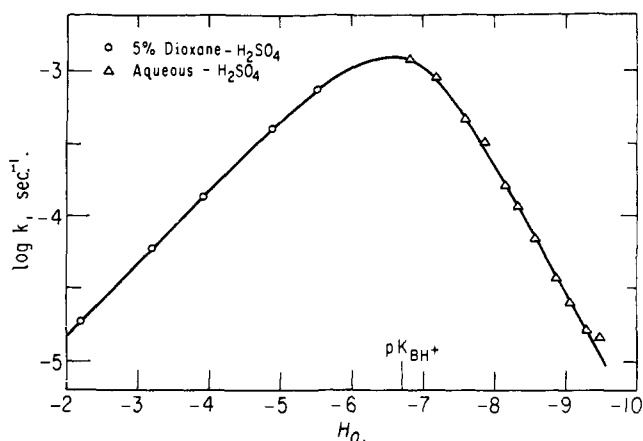


Fig. 1.—Rate of isomerization of *cis*-4-nitrochalcone.

temperature to about 5° the rate of isomerization is sufficiently slowed that  $pK$  measurements are reasonably convenient and do not require any substantial extrapolation to zero time. The basicity constant for *cis*-4-nitrochalcone,  $pK_{BH^+}$ , at 5° is  $-6.75$  on the  $H_0$  scale. We have used this value without making any correction for the difference in temperature, as it is well known that dissociation constants are not unduly sensitive to temperature changes.

TABLE I  
RATE OF ISOMERIZATION OF *cis*-*p*-NITROCHALCONE IN AQUEOUS SULFURIC ACID AT 25.00°

H <sub>2</sub> SO <sub>4</sub> , %	H <sub>0</sub> <sup>c</sup>	k <sub>1</sub> , sec. <sup>-1</sup>	Corrected <sup>d</sup> k, sec. <sup>-1</sup>	log a <sub>H<sub>2</sub>O</sub>
9.24 <sup>a,b</sup>	-0.20	$5.8 \times 10^{-7}$		
37.68 <sup>b</sup>	-2.19	$1.90 \times 10^{-6}$		
46.62 <sup>b</sup>	-4.82	$4.00 \times 10^{-4}$		
78.20	-6.75	$1.22 \times 10^{-3}$	$2.44 \times 10^{-3}$	-2.07
81.40	-7.16	$8.88 \times 10^{-4}$	$1.23 \times 10^{-3}$	-2.42
83.81	-7.48	$4.53 \times 10^{-4}$	$5.39 \times 10^{-4}$	-2.75
86.13	-7.80	$3.04 \times 10^{-4}$	$3.31 \times 10^{-4}$	-3.075
86.50	-7.85	$2.57 \times 10^{-4}$	$2.78 \times 10^{-4}$	-3.12
88.26	-8.05	$1.60 \times 10^{-4}$	$1.68 \times 10^{-4}$	-3.38
90.26	-8.26	$1.13 \times 10^{-4}$	$1.76 \times 10^{-4}$	-3.66
92.09	-8.53	$6.56 \times 10^{-5}$	$6.65 \times 10^{-5}$	-3.98
94.30	-8.80	$3.59 \times 10^{-5}$	$3.62 \times 10^{-5}$	-4.36
95.75	-8.95	$2.41 \times 11^{-6}$	$2.41 \times 11^{-6}$	-4.62
97.26	-9.20	$1.60 \times 10^{-5}$	$1.60 \times 10^{-5}$	-5.03
98.25	-9.40	$1.48 \times 10^{-5}$	$1.48 \times 10^{-5}$	-5.41

<sup>a</sup> Extrapolated from previous data. <sup>b</sup> From previous data, 5% dioxane solvent mixture. <sup>c</sup> All  $H_0$  values are from Long and Paul (*Chem. Rev.*, **57**, 1 (1957)). <sup>d</sup> Corrected for fraction not protonated.

Above 78% sulfuric acid, an increase in the acid concentration in the reaction medium results in a decrease in rate, rather than an increase, as shown in Table I and Fig. 1. Once the chalcone is largely converted to the conjugate acid, a further increase in the acid concentration will not raise the rate; on the contrary, the concomitant decrease in the activity of water will lower the observed rate of isomerization. This is the observed result in the present instance. From 78% sulfuric acid to 95% sulfuric acid there is a decrease in the observed rate of isomerization of a factor of 100. This decrease in rate very closely parallels the decreasing activity of water in this region of sulfuric acid concentration. These observations are in complete accord with the mechanism of isomerization suggested earlier,<sup>6</sup> in which the rate-determining step is the attack of water at the  $\beta$ -carbon of the conjugate acid of the chalcone (eq. 2).

**The Question of General Catalysis.**—The requirements of mechanism A for both an acid and a nucleo-

phile suggest that this mechanism properly belongs in the category of those which show general acid catalysis. It would be expected, therefore, that other nucleophiles (e.g., bisulfate ion) could compete with water under the appropriate conditions. In fact, we have noted earlier<sup>4</sup> that sulfuric acid is somewhat more effective as a catalyst than is perchloric acid of the same  $H_0$  value. Additionally, in acetic acid solution a rate of isomerization was observed which was in excess of that which could be ascribed to the acidity of the solution, *i.e.*, a rate due to molecular acetic acid. There is thus a reasonable amount of evidence that is consistent with general acid catalysis.

Several recent investigations have examined the possibility of general catalysis in very concentrated sulfuric acid. Swain and Rosenberg<sup>8</sup> have shown that the rate of enolization of  $\alpha$ -phenylisocaprophenone decreases in the region of 85–93% sulfuric acid, and that it appears that bisulfate ion is about one-hundredth as effective as water as a nucleophile in this region. Schubert and Burkett<sup>9</sup> have discussed the role of acid-base catalysis in the decarbonylation reaction of aromatic aldehydes. Brand<sup>10</sup> and Deno and Taft<sup>11</sup> have suggested that the concentration of available water and bisulfate ion may be closely approximated in 85–100% sulfuric acid and that the activity coefficients of the various species are nearly invariant in this region.

The present data may be analyzed in terms of both water and bisulfate ion acting as nucleophiles to add to the  $\beta$ -carbon (eq. 4). Calculated in this fashion,  $k_{H_2SO_4}$  is one-fiftieth of  $k_{H_2O}$ . In 80% sulfuric acid,

$$k_{total} = k_{H_2O}[H_2O] + k_{HSO_4^-}[HSO_4^-] \quad (4)$$

this leads to the conclusion that practically all of the reaction proceeds *via* nucleophilic attack by water on the conjugate acid of *cis*-4-nitrochalcone; while in 97% sulfuric acid, some 75% of the total reaction is proceeding by way of nucleophilic attack by bisulfate ion.

The simple beauty of this pattern of interpretation is considerably beclouded by one additional consideration. The isomerization by mechanism B does not involve a nucleophile; it is a reaction in which the activated complex consists only of a proton and the organic molecule. It, therefore, follows, assuming constant activity coefficients in the 85–100% sulfuric acid region, that the observed rate of isomerization by way of mechanism B should become constant in this region once protonation is complete. This is not, in fact, exactly correct. The data for three compounds (*vide infra*) show a small, but definite increase in the rate of reaction by mechanism B in the 80–100% sulfuric acid region. Furthermore, comparison of the concentration of "free water" as determined by the approximate method of Brand<sup>10</sup> and Deno and Taft<sup>11</sup> with the activity of water as recently reported by Giauque, Horning, Kunzler, and Rubin<sup>12</sup> shows that the activity coefficient of water is not invariant in this region, but does change modestly. Clearly then, the sequence of arguments necessary to arrive at the rate of the bisulfate ion assisted isomerization of *cis*-4-nitrochalcone is not rigorous but only approximate.

Our present interpretation is that the role of general acid-catalyzed reactions in the concentrated sulfuric acid region needs a great deal more study before positive conclusions regarding mechanism may be drawn from a single set of data.

(8) C. G. Swain and A. S. Rosenberg, *J. Am. Chem. Soc.*, **83**, 2154 (1961).

(9) W. M. Schubert and H. Burkett, *ibid.*, **78**, 64 (1956).

(10) J. C. D. Brand, *J. Chem. Soc.*, 1002 (1950).

(11) N. C. Deno and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **76**, 244 (1954).

(12) W. F. Giauque, E. W. Horning, J. E. Kunzler, and T. R. Rubin, *ibid.*, **82**, 62 (1960).

TABLE II  
SOLVENT ISOTOPE EFFECT ON THE RATE OF ISOMERIZATION OF  
*cis*-4-NITROCHALCONE IN 86% SULFURIC ACID

Acid	$k$ , sec. <sup>-1</sup>	$k_H/k_D$ , wt. % <sup>a</sup>	$k_H/k_D$ mole fraction <sup>b</sup>
85.90% D <sub>2</sub> SO <sub>4</sub>	$1.99 \times 10^{-4}$		
85.90% H <sub>2</sub> SO <sub>4</sub>	$3.16 \times 10^{-4c}$	1.58	
86.90% H <sub>2</sub> SO <sub>4</sub>	$2.40 \times 10^{-4c}$		1.20

<sup>a</sup> Compared on a wt. % basis. <sup>b</sup> Compared on a mole fraction basis,  $N_{SO_4^{2-}} = 0.549$ . <sup>c</sup> Interpolated from the data in Table I.

**Solvent Isotope Effect.**—When the isomerization of *cis*-4-nitrochalcone is carried out in 86% deuteriosulfuric acid, the rate of isomerization is somewhat less than in the corresponding protium solvent (Table II).

The observed value of  $k_H/k_D$  is in good agreement with the ratio calculated from the measured isotope effects in dilute solution for chalcone,<sup>5</sup>  $k_H/k_D$  1.92, and for 4-methoxychalcone,<sup>6</sup>  $k_H/k_D$  2.82. Since 4-methoxychalcone isomerizes by a unimolecular mechanism not involving water in the transition state (eq. 3), the value 2.8 represents the effect of D<sub>2</sub>SO<sub>4</sub> on the protonation equilibrium alone (eq. 1) for chalcones acting as bases. It can then be concluded that in the bimolecular mechanism of isomerization the value of 1.92 for chalcone is a composite of the isotope effect of the prior equilibrium and that of the subsequent rate-determining step involving the nucleophilic attack of water on the conjugate acid of the chalcone (eq. 2). The value calculated for the  $k_H/k_D$  solvent isotope effect of the latter step is 1.47, in fair agreement with the observed value of 1.20 for *cis*-4-nitrochalcone in 86% acid. This isotope effect is in accord with reported values of solvent isotope effects in reactions involving water in the transition state.<sup>13-16</sup> The value of 1.20 in the present case represents the order of magnitude of isotope effect to be expected,<sup>15</sup> but not previously reported for a rate-determining nucleophilic attack of water on an olefinic bond. Since the degree of carbon-oxygen bond formation in the transition state of this reaction is relatively small (as inferred from substituent effects, *vide infra*), this value is probably near the lower limit of the range of isotope effects describing such a reaction.

***cis*-Chalcone.**—In the 70–98% sulfuric acid region, the rate of isomerization of *cis*-chalcone shows a complex profile (Table III and Fig. 2). The rate is a maximum at the  $pK$  for *cis*-chalcone (–5.87) and then decreases regularly, closely paralleling the activity of water to 88% sulfuric acid. Concentrations greater than 88% sulfuric acid result in a small, but definite increase, the rate doubling from 88 to 98% acid.

TABLE III  
ISOMERIZATION OF *cis*-CHALCONE IN CONCENTRATED AQUEOUS  
SULFURIC ACID AT 25.00°

H <sub>2</sub> SO <sub>4</sub> , %	$k_1$ , sec. <sup>-1a</sup>	$H_0$
70.63	$7.00 \times 10^{-3}$	–5.70
72.22	$7.97 \times 10^{-3}$	–5.92
78.20	$3.19 \pm 0.11 \times 10^{-3b}$	–6.72
81.40	$1.93 \times 10^{-3}$	–7.18
83.40	$1.37 \pm 0.03 \times 10^{-3b}$	–7.44
88.26	$9.36 \pm .12 \times 10^{-4b}$	–8.05
92.10	$1.06 \pm .02 \times 10^{-3b}$	–8.53
95.75	$1.44 \pm .01 \times 10^{-3b}$	–8.95
98.25	$1.86 \times 10^{-3}$	–9.45

<sup>a</sup> Method III. <sup>b</sup> Average of 2 runs.

(13) T. Riley and F. A. Long, *J. Am. Chem. Soc.*, **84**, 522 (1962); F. A. Long and D. Watson, *J. Chem. Soc.*, 2019 (1958).

(14) M. L. Bender, E. J. Pollock, and M. C. Neveu, *J. Am. Chem. Soc.*, **84**, 594 (1962).

(15) C. G. Swain and E. R. Thornton, *ibid.*, **84**, 817, 822 (1962).

(16) V. Gold and A. R. Butler, *Proc. Chem. Soc.*, 15 (1960); *J. Chem. Soc.*, 2305, 4362 (1961).

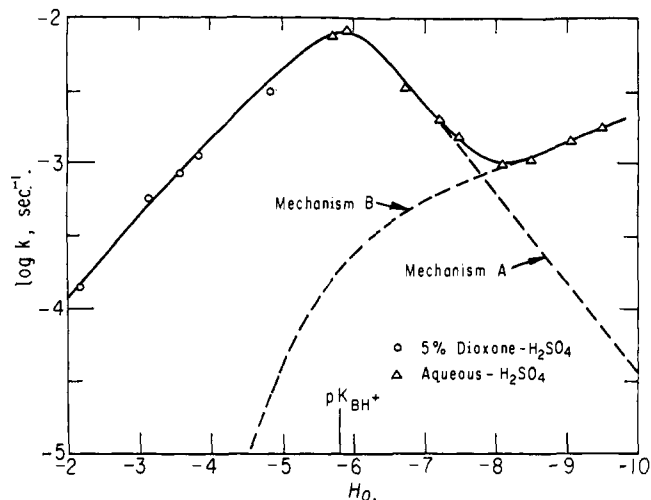


Fig. 2.—Rate of isomerization of *cis*-chalcone at 25.00°.

The only satisfactory interpretation of this change is in terms of a change from mechanism A to mechanism B, with the two mechanisms being equally effective at 88% acid and mechanism B dominant in sulfuric acid concentrations greater than 88%. The total shape of the rate profile cannot be explained in terms of both water and bisulfate ion acting as nucleophiles, as the concentration of both species decreases substantially from 88 to 98% sulfuric acid.

A further point of interpretation is important to the foregoing discussion. The rate of isomerization by mechanism B, were it to show "ideal" behavior, should be constant in this region (88–98% sulfuric acid) as the *cis*-chalcone is completely protonated.

The very slightly positive slope ( $\sim 0.2$ ) shows that in this region the behavior of the conjugate acid of *cis*-chalcone is not ideal, and that the assumption of unchanging activity coefficients is only approximate (*vide supra*).

***o*-Substituted Chalcones.**—The introduction of a substituent in the *o*-position should reduce the facility of the addition of water at the  $\beta$ -carbon in mechanism A. With this purpose in mind, we have examined the rate of isomerization of *cis*-2-chlorochalcone (IX) (Table IV) and *cis*-2-methylchalcone (X) (Table V).

The isomerization of *cis*-2-chlorochalcone (IX) shows the same type of complex rate profile observed with *cis*-

TABLE IV  
ISOMERIZATION OF *cis*-2-CHLOROCHALCONE,  $T = 25.00^\circ$

H <sub>2</sub> SO <sub>4</sub>	$k_1$ , sec. <sup>-1</sup>	$H_0$
5% dioxane–95% aqueous sulfuric acid		
6.16 M <sup>a</sup>	$3.85 \times 10^{-5}$	–2.90
7.96 M <sup>a</sup>	$9.62 \times 10^{-5}$	–4.00
8.69 M <sup>a</sup>	$1.80 \times 10^{-4}$	–4.44
9.93 M <sup>a</sup>	$3.35 \times 10^{-4}$	–5.15
68.2% <sup>a</sup>	$6.19 \times 10^{-4}$	–5.70
69.4% <sup>a</sup>	$7.96 \times 10^{-4}$	–5.90
71.2% <sup>b</sup>	$8.56 \times 10^{-4}$	–6.20
75.6% <sup>b</sup>	$7.25 \pm 0.50 \times 10^{-4c}$	–6.80
80.5% <sup>b</sup>	$3.50 \times 10^{-4}$	–7.40
Aqueous sulfuric acid		
77.75% <sup>a</sup>	$5.50 \times 10^{-4}$	–6.75
82.7% <sup>a</sup>	$2.14 \times 10^{-4}$	–7.35
84.3% <sup>a</sup>	$1.24 \times 10^{-4}$	–7.62
87.6% <sup>a</sup>	$9.39 \times 10^{-5}$	–7.97
91.9% <sup>a</sup>	$5.45 \times 10^{-5}$	–8.49
96.1% <sup>a</sup>	$7.70 \times 10^{-5}$	–9.01
98.6% <sup>a</sup>	$1.39 \times 10^{-4}$	–9.52

<sup>a</sup> Method I, 10-cm. cells. <sup>b</sup> Method II, 1-cm. cell. <sup>c</sup> Average of 2 values.

TABLE V  
 ISOMERIZATION OF *cis*-2-METHYLCHALCONE,  $T = 25.00^\circ$ 

H <sub>2</sub> SO <sub>4</sub>	$k_1$ , sec. <sup>-1</sup>	H <sub>0</sub>
5% dioxane-95% aqueous sulfuric acid		
6.17 <i>M</i> <sup>a</sup>	$1.41 \times 10^{-4}$	-2.90
7.51 <i>M</i> <sup>a</sup>	$3.04 \times 10^{-4}$	-3.74
8.17 <i>M</i> <sup>a</sup>	$5.50 \times 10^{-4}$	-4.13
8.87 <i>M</i> <sup>a</sup>	$7.96 \times 10^{-4}$	-4.56
9.38 <i>M</i> <sup>a</sup>	$1.28 \times 10^{-3}$	-4.84
65.7% <sup>b</sup>	$2.46 \times 10^{-3}$	-5.40
68.2% <sup>b</sup>	$2.90 \pm 0.08 \times 10^{-3c}$	-5.72
69.7% <sup>b</sup>	$3.11 \pm .04 \times 10^{-3c}$	-5.92
73.6% <sup>b</sup>	$3.59 \pm .16 \times 10^{-3c}$	-6.60
76.2% <sup>b</sup>	$5.16 \pm .11 \times 10^{-3d}$	-6.92
79.3% <sup>b</sup>	$5.85 \pm .07 \times 10^{-3c}$	-7.30
Aqueous sulfuric acid		
76.5% <sup>b</sup>	$5.78 \pm 0.24 \times 10^{-3c}$	-6.50
78.2% <sup>b</sup>	$5.77 \times 10^{-3c}$	-6.72
83.4% <sup>b</sup>	$8.25 \times 10^{-3c}$	-7.42
88.3% <sup>b</sup>	$9.90 \times 10^{-3}$	-8.05
92.1% <sup>b</sup>	$1.50 \pm 0.10 \times 10^{-2d}$	-8.50
96.4% <sup>b</sup>	$1.72 \pm 0.06 \times 10^{-2c}$	-9.00
97.3% <sup>b</sup>	$1.78 \times 10^{-2}$	-9.20

<sup>a</sup> Method I, 10-cm. cell. <sup>b</sup> Method III, 1-cm. cell. <sup>c</sup> Average of 2 values. <sup>d</sup> Average of 3 values.

chalcone. A maximum in rate is observed at about 75% sulfuric acid, very close to the calculated  $pK_{BH^+}$  for IX. As the acid concentration is increased, the rate decreases, and a minimum in rate is reached at 92% sulfuric acid. More concentrated sulfuric acid results finally in a small increase in rate, about a factor of 2.5 from 92 to 98% sulfuric acid. This latter region represents isomerization by mechanism B.

The isomerization of *cis*-2-methylchalcone follows the same pattern, but the quantitative relationships between the rates for isomerization by mechanism A or mechanism B are substantially changed. The rate of isomerization of X increases regularly from dilute sulfuric acid to 68% sulfuric acid; at the  $pK$  for *cis*-2-methylchalcone (estimated to be -5.72) the rate profile appears to level and then shows a slow gradual rise to 98% acid. In the case of X, the change from mechanism A to the carbonium ion mechanism (mechanism B) has occurred in the region of acidity almost coincident with the  $pK$  for X. We thus see the combination of two factors, the *o*-substituent hindering mechanism A and the electron-donating capabilities of the methyl group favoring mechanism B.

**Isomerization of *cis*-2,4-Dimethoxychalcone.**—The rate of the acid-catalyzed isomerization of *cis*-2,4-dimethoxychalcone was determined in dilute sulfuric acid. It quickly became apparent that the rate of isomerization was very high. It was particularly convenient to follow the kinetics by the procedure using the photodynamic equilibrium mixture rich in the *cis* isomer. In this procedure a sample of the *trans*-chalcone in dilute aqueous sulfuric acid was briefly irradiated to prepare the photodynamic mixture of the *cis* and *trans* isomers of XII and the kinetics of isomerization measured directly. Data obtained at 25 and 45° are given in Table VI.

The isomerization is strongly acid catalyzed; a plot of the logarithm of the observed rate *vs.* pH shows a slope just slightly greater than one. Several experiments have been carried out to show that the mechanism of isomerization is the same as that of *cis*-4-methoxychalcone. When a dilute solution of *trans*-2,4-dimethoxychalcone in dioxane was irradiated (conversion of about 80% to the *cis* isomer) and allowed to stand in contact with an equal volume of 1 *M* deuteriosulfuric acid in deuterium oxide, the *trans*-2,4-dimethoxychalcone recovered showed the

 TABLE VI  
 RATE OF ISOMERIZATION OF *cis*-2,4-DIMETHOXYCHALCONE IN 5% DIOXANE-AQUEOUS SULFURIC ACID

H <sub>2</sub> SO <sub>4</sub> , <i>M</i>	$k \times 10^4$ , sec. <sup>-1a</sup>	pH	log $k + pH$
25.00°			
0.00174 <sup>d</sup>	1.24	2.44	-1.47
.00380 <sup>d</sup>	2.31	2.23	-1.40
.0104	5.63	1.82	-1.43
.0277	14.1	1.41	-1.44
.0340	17.2	1.32	-1.44
.0522	$28.2 \pm 0.2^b$	1.18	-1.37
.0801	$38.7 \pm .2^b$	1.00	-1.41
.1025	$51.0 \pm .3^b$	0.95	-1.34
.1605	$80.1 \pm 1.4^b$	0.75	-1.34
45.00°			
0.00174 <sup>d</sup>	$6.51 \pm 0.09^b$		
0.00380 <sup>d</sup>	$12.7 \pm 0.4^c$		

<sup>a</sup> Method I (ref. 1), 10-cm. cells. <sup>b</sup> Average of 2 runs. <sup>c</sup> Average of 4 runs. <sup>d</sup>  $E_a = 15.85$  kcal.,  $\Delta H^\ddagger = 15.25$  kcal.,  $\Delta S^\ddagger = -13.5$  e.u.

absence of deuterium bands in the infrared spectrum. Further, the activation entropy compares favorably with the results obtained earlier for *cis*-4-methoxychalcone.<sup>4</sup> The necessary extrapolation from very dilute sulfuric acid to 1 *M* sulfuric acid introduces some uncertainty in the values of the activation parameters.

These facts support the conclusion that the mechanism of isomerization of XII is the same as that of *cis*-4-methoxychalcone, in which the rate-determining process is the unimolecular isomerization of the conjugate acid of the *cis*-chalcone.

**Isomerization of *cis*-2,4,6-Trimethoxychalcone.**—A similar set of information (Table VII) showed that the isomerization of *cis*-2,4,6-trimethoxychalcone is consistent in all respects with mechanism B. The rate increases smoothly with increased acid concentration; the entropy of activation (calculated from the rate extrapolated to 1 *M* sulfuric acid) is only slightly negative, consistent with an activated complex built up of the reacting organic molecule and a proton. As a further check, the isomerization was carried out in deuteriosulfuric acid. The infrared spectrum of the sample of *trans*-XIV isolated was identical in all respects with an authentic sample of XIV, but was distinctly different from a sample of 2,4,6-trimethoxychalcone- $\alpha$ -*d*<sub>1</sub> prepared from trimethoxybenzaldehyde and acetophenone-*d*<sub>3</sub>.

 TABLE VII  
 RATE OF ISOMERIZATION OF *cis*-2,4,6-TRIMETHOXYCHALCONE IN 5% DIOXANE-AQUEOUS SULFURIC ACID

pH <sup>a</sup>	$k \times 10^4$ , sec. <sup>-1b</sup>	log $k + pH$
$T = 25.00^\circ$		
3.48	0.888	-0.57
3.24 ( $2.85 \times 10^{-4}$ <i>M</i> ) <sup>d</sup>	1.71	-.52
2.50	9.17	-.54
2.23	$18.9 \pm 0.3^c$	-.49
1.82	$48.2 \pm 0.2^c$	-.50
$T = 45.00^\circ$		
H <sub>2</sub> SO <sub>4</sub> , <i>M</i>		
$2.85 \times 10^{-4d}$	$9.71 \pm 0.08^c$	
$4.20 \times 10^{-4}$	$17.2 \pm 0.2^c$	

<sup>a</sup> The pH of the 5% dioxane-aqueous sulfuric acid was measured. <sup>b</sup> The kinetic measurements were made by method I. <sup>c</sup> Average of 2 runs. <sup>d</sup>  $E_a = 16.4$  kcal.,  $\Delta H^\ddagger = 15.8$  kcal.,  $\Delta S^\ddagger = -7.4$  e.u.

It is to be noted that the treatment of XIV with more concentrated deuteriosulfuric acid does result in a marked spectral change; this is probably the result of exchange of deuterium for hydrogen in the activated ring.

**Isomerization of *cis*-2,6-Dimethoxychalcone (XIII).**—The presence of the two methoxyl groups flanking the  $\beta$ -carbon of the olefinic system results in isomerization by mechanism B, but a rate of reaction (Table VIII) which is quite low in dilute acid solution. The rate of reaction becomes rapid in 30% sulfuric acid solution.

TABLE VIII

RATE OF ISOMERIZATION OF *cis*-2,6-DIMETHOXYCHALCONE IN 5% DIOXANE-AQUEOUS SULFURIC ACID

$H_2SO_4, M$	$H_0$	$k_1 \times 10^4, \text{sec.}^{-1a}$		$\log k + H_0$
		25.00°		
2.83 <sup>b</sup>	-1.15	0.385	-5.57	
3.91	-1.68	2.10	-5.36	
4.27	-1.85	4.12	-5.23	
4.83	-2.12	9.24	-5.15	
5.42	-2.42	27.2	-4.98	
		45.00°		
2.83 <sup>b</sup>	-1.15	4.36		

<sup>a</sup> All measurements were made by method II. <sup>b</sup>  $E_a = 22.9$  kcal.,  $\Delta H^\ddagger = 22.3$  kcal.,  $\Delta S^\ddagger = -9.4$  e.u.

### Discussion

#### Sensitivity of Mechanism A to Substituent Effects.

The accumulated rate data for a wide variety of substituents allow comparison of the rates of attack by water on the conjugate acids of the *cis*-chalcones. For *cis*-chalcone, *cis*-4-nitrochalcone, and *cis*-2-chlorochalcone these rates are directly available from the experimental measurements (Table IX). It is only necessary to make a judicious choice of acidity conditions for this comparison.

TABLE IX

RATE CONSTANTS FOR ISOMERIZATION OF THE CONJUGATE ACIDS OF SUBSTITUTED *cis*-CHALCONES *via* MECHANISM A AT 25°

Substituent	$k_1 a_{H_2O}^w, \text{sec.}^{-1}$		$pK_{BH^+}^c$
	$H_0 = -6.6^a$	$H_0 = -2.0^b$	
H	$4.0 \times 10^{-3}$	92	-5.87
4-CH <sub>3</sub>		59	-5.49
4-Cl		72	-6.04
4-NO <sub>2</sub>	$4.0 \times 10^{-3}$	120	-6.92
2-OCH <sub>3</sub>		28 <sup>d</sup>	-5.33
2-CH <sub>3</sub>	$1.0 \times 10^{-3e}$	27	-5.72
2-Cl	$1.0 \times 10^{-3}$	40	-6.43

<sup>a</sup> These values are obtained directly from reported rates in concentrated aqueous sulfuric acid, corrected for any small fraction of unprotonated base present. <sup>b</sup> Obtained by multiplying the observed rate by  $K_{BH^+}$  both as measured in 5% dioxane-95% aqueous sulfuric acid. <sup>c</sup> The  $pK_{BH^+}$  values of the *cis* isomers are taken to be uniformly less basic by 0.70 unit than the *trans* isomer in 5% dioxane-95% aqueous sulfuric acid. <sup>d</sup> From data given in the following paper. <sup>e</sup> Rate was calculated by subtracting the calculated rate for mechanism B, at the same acidity, from the observed rate; it is also corrected to purely aqueous sulfuric acid from the 5% dioxane medium used experimentally.

The data show that the rate constant at  $H_0 = -6.6$  is nearly the same for all chalcones, being quite insensitive to the nature of the substituent in the ring.

Comparisons with other chalcones may be made in more dilute sulfuric acid. The best procedure for such comparison is to take a common acidity and make a correction for the fraction of the chalcone which is protonated, using measured or estimated basicities for the *cis*-chalcones. In a previous paper<sup>1</sup> we have determined some of these basicities and have estimated others based on the general patterns shown in those studies (column 4, Table IX). In this fashion a cohesive set of information, the rate of attack by water on the conjugate acid of the *cis*-chalcone in 34% sulfuric acid, may be obtained (column 3, Table IX). Again, a considerable similarity in rate constants is observed. The rate constant for *cis*-4-nitrochalcone is somewhat larger than

the others. *o*-Substituted chalcones give somewhat smaller rates, exhibiting a very modest retardation. These observations are in accord with the conclusion that the transition state for the isomerization by mechanism A largely resembles the conjugate acid of the *cis*-chalcone, with the carbon-oxygen bond being formed by the attacking water still long and weak.

#### Sensitivity of Mechanism B to Substituent Effects.

Mechanism B is extremely sensitive to the effects of substituents. Comparisons have been made in dilute sulfuric acid for the methoxychalcones by extrapolating the rates to common conditions. The rates of isomerization by mechanism B for a wider variety of substituted chalcones can be compared in the very high acidity region.

A summary of the observed rates of isomerization for methoxychalcones, extrapolated both to 1 *M* and to 4.5 *M* sulfuric acid, is presented in Table X. The dramatic change in the rate of reaction caused by the introduction of two or three methoxyl groups is clearly evident. The rate increase resulting from the introduction of a 4-methoxyl group is  $2 \times 10^5$  (comparison of *cis*-2,6-dimethoxychalcone and *cis*-2,4,6-trimethoxychalcone). Comparison of the rates for *cis*-chalcone and *cis*-4-methoxychalcone cannot be made directly, as *cis*-chalcone isomerizes by mechanism A in dilute sulfuric acid. If one makes the extremely severe extrapolation from 90% sulfuric acid to 1 *M* sulfuric acid in order to estimate the rate of isomerization by mechanism B for *cis*-chalcone, the rate ratio of *cis*-4-methoxychalcone to *cis*-chalcone is about  $10^6$ . A very similar ratio results by making the extrapolation of the rate of isomerization of *cis*-2-methoxychalcone by mechanism B and comparing it with the rate for *cis*-2,4-dimethoxychalcone.

TABLE X

RELATIVE RATES FOR ISOMERIZATION OF VARIOUS METHOXYCHALCONES AT 25°

Substituted chalcone	$\log k, \text{sec.}^{-1}$ at 1 <i>M</i> H <sub>2</sub> SO <sub>4</sub>	Relative rate	$\log k, \text{sec.}^{-1}$ at 4.5 <i>M</i> H <sub>2</sub> SO <sub>4</sub> ( $H_0 = -2.0$ )	
			Relative rate	Relative rate
H	-5.28	3.2	-4.03	1
4-OCH <sub>3</sub>	-4.18	40	-1.93	125
2-OCH <sub>3</sub>	-5.38	2.5	-3.83	1.6
2,4-(OCH <sub>3</sub> ) <sub>2</sub>	-1.35	27,000	+1.00	105,000
2,6-(OCH <sub>3</sub> ) <sub>2</sub>	-5.78	1	-3.23	6.3
2,4,6-(OCH <sub>3</sub> ) <sub>3</sub>	-0.40	240,000	+2.20	1,700,000

A more extensive comparison of relative rates may be made by calculating the rate of isomerization of the salt of the *cis*-chalcones by mechanism B; these rates correspond to the rate of rotation about the "allylic" bond in the protonated chalcone. Such a comparison can be made by correcting the observed rates for the prior protonation equilibrium at  $H_0 = 0$ , or, alternatively, by comparing rates at high acidities where protonation is complete. The latter is preferred.<sup>17</sup>

The entire set of information is presented in Table XI. Again, the extremely high sensitivity of mechanism B to the effect of substituents is noted, the total rate range covering twelve decades. These rate constants are obtained directly in the case of chalcone, *cis*-2-methyl-

(17) The standard for comparison was chosen as that acidity at which protonation is 99% complete; this choice is necessitated by the fact that the rates are not completely invariant with further increases in acid concentration. Several extrapolations are required to obtain all of the rates under these conditions. Such extrapolations were carried out, constructing a complete rate- $H_0$  profile, using the measured slopes and the  $pK$  values for the *cis* isomers. Many of these were measured, others were estimated. Specifically the  $pK$  values of *cis*-2,4- and *cis*-2,6- were calculated on the basis of the additivity of the effect of substituents on  $pK$ , using a  $\sigma^-$ -value of  $-0.5$  for the *o*-methoxy group. A few of the extrapolations are extremely severe, obviously these rates are subject to substantial uncertainties.

chalcone, and *cis*-2-chlorochalcone. The isomerization of *cis*-4-nitrochalcone proceeds by the water addition mechanism in the region of 90–98% sulfuric acid, which clearly means that the carbonium ion mechanism has a rate of less than  $10^{-7}$  sec.<sup>-1</sup>. For *cis*-4-methylchalcone the rate constant is less precise as the change to mechanism B occurs at an acidity corresponding to an exceedingly fast reaction rate.

TABLE XI

UNIMOLECULAR RATE CONSTANTS FOR THE ISOMERIZATION OF THE CONJUGATE ACIDS OF SUBSTITUTED CHALCONES *via* MECHANISM B AT 25°

Substituent	$k_1$ , sec. <sup>-1a</sup>	Relative rates
H	$8.0 \times 10^{-4b}$	10 <sup>6</sup>
4-OCH <sub>3</sub>	$1.6 \times 10^{2c}$	10 <sup>10</sup>
4-CH <sub>3</sub>	$1.0 \times 10^{-1d,e}$	10 <sup>7</sup>
4-Cl	$1.6 \times 10^{-4d}$	10 <sup>4</sup>
4-NO <sub>2</sub>	$\sim 10^{-8f}$	1
2-OCH <sub>3</sub>	$2.5^{c,e}$	10 <sup>8</sup>
2-CH <sub>3</sub>	$1.0 \times 10^{-2b}$	10 <sup>6</sup>
2-Cl	$4.0 \times 10^{-5f}$	$5 \times 10^2$
2,4-(OCH <sub>3</sub> ) <sub>2</sub>	$3.2 \times 10^{4g}$	$3 \times 10^{12}$
2,6-(OCH <sub>3</sub> ) <sub>2</sub>	20 <sup>h</sup>	$2 \times 10^9$
2,4,6-(OCH <sub>3</sub> ) <sub>3</sub>	$3.0 \times 10^{5h}$	$3 \times 10^{13}$

<sup>a</sup> Calculated at 99% protonation. <sup>b</sup> Rate constants obtained by direct measurement in aqueous sulfuric acid. <sup>c</sup> Rate constants obtained by constructing a theoretical curve across the protonation region with data and slopes (1.26) from lower acidities<sup>6</sup> in 5% dioxane–95% aqueous sulfuric acid. <sup>d</sup> Calculated values on the basis of  $\rho = -7$ . <sup>e</sup> Data tabulated in the following paper. <sup>f</sup> Rate constants obtained by constructing a theoretical curve from the observed rates for this mechanism at the highest acidities and from the  $pK_{BH^+}$  [=  $pK_{trans} - (-0.7)$ ] in aqueous sulfuric acid. <sup>g</sup> Calculated by constructing a theoretical curve, using a slope above  $H_0 = 0$  of 1.25 and a calculated  $pK$  value of  $-4.2$ . <sup>h</sup> Calculated by constructing a theoretical curve, using a slope of 1.40, above  $H_0 = 0$ , a  $pK$  of  $-3.45$  for *cis*-2,4,6-trimethoxychalcone, and a calculated  $pK$  of  $-4.6$  for *cis*-2,6-dimethoxychalcone.

From the data reported in Table XI, omitting the less reliable rates for the polymethoxychalcones, a  $\rho$ -value of approximately  $-7$  can be calculated from a  $\sigma^+\rho$  correlation. This very negative  $\rho$ -value is in full accord with the mechanism and the mechanistic deductions reached earlier. The activated complex was described as having a full positive charge localized at a benzylic position, since the two halves of the molecule are oriented in planes orthogonal to each other.

For reactions involving benzyl carbonium ion intermediates, negative  $\rho$ -values are typical, though generally of lesser magnitude.<sup>18</sup> The largest value reported,

(18) The solvolyses of cumyl halides in aqueous acetone give a  $\rho$  of  $-4.54$  (H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958)), of benzyl tosylates in acetic acid a  $\rho$  of about 5 (G. S. Hammond, C. E. Reeder, F. T. Faug, and J. K. Kochi, *ibid.*, **80**, 568 (1958)), and the ionization of diarylcarbinols in sulfuric acid gives a  $\rho$  of  $-4.74$  (N. C. Deno and A.

$-20$ , is that observed by Lossing,<sup>19</sup> for the ionization potentials for substituted benzyl radicals. The solvolyses of benzyl mercuric cations has recently been reported to give a  $\rho$  of  $-7$ .<sup>20</sup>

**Effect of Substituents in the *o*-Position.**—From the rate constants presented in Table IX it becomes evident that the principal factor responsible for the decreased rate of isomerization *via* mechanism A is the decreased basicity of the *o*-substituted chalcone. There is only a factor of two between any *ortho-para* pair of *cis*-chalcones which can be attributed to a steric effect by the substituent reducing the rate of attack by water at the  $\beta$ -carbon.

Examination of the effect of *o*-substituents on mechanism B needs explanation. The smaller influences on the rates are accounted for by a diminished effective value of  $\sigma^+$ -constants for *o*-substituents. These values are not available but can be estimated from the data on basicities of chalcones which we have previously reported.<sup>1</sup> The  $\sigma^+\rho$  relationship of *trans-p*-substituted chalcones permits the estimation of  $\sigma^+$ -values of the *o*-methoxy and *o*-methyl substituent, respectively,<sup>21</sup> accounting well for the observed *para-ortho* rate ratios of 100 and 10 for the methoxy and methyl groups, respectively.<sup>22</sup> It can thus be concluded that steric effects to rotation around the allylic bond (mechanism B) from an *o*-substituent are absent.<sup>23</sup>

**Stability of Allylic Cations.**—Finally, these data provide further insight into the stability of allylic cations. As described previously,<sup>4</sup> the conjugate acids of the *cis*-chalcones contain among the canonical resonance structures an "allylic pair." The introduction of methoxyl groups greatly reduces the double bond character in the  $C_\alpha-C_\beta$  bond, as reflected in the increased rate of the unimolecular isomerization. As the data in Table XI show, the half-life for the cation is reduced from 1 hr. in the case of *cis*-chalcone to milliseconds for trimethoxychalcone. The free energy of activation for the isomerization decreases from 22 to 10 kcal.

Schriesheim, *ibid.*, **77**, 3051 (1955); N. C. Deno and W. L. Evans, *ibid.*, **79**, 5804 (1957).

(19) A. G. Harrison, P. Kebarle, and F. P. Lossing, *ibid.*, **83**, 777 (1961).

(20) F. R. Jensen, G. Knutson, D. Babbe, and R. J. Oullette, Abstracts of Papers, 144th National Meeting, American Chemical Society, Los Angeles, Calif., April, 1963, p. 29M.

(21) An alternative estimation of the value for the *o*-methoxy group from the  $\rho$  of  $-7$  and from the observed differences in rate of a factor of 3000 between *o*-methoxychalcone and chalcone also leads to the same  $\sigma^+$ -value.

(22) The small *ortho-para* ratio of 4 for the chlorochalcone is not as satisfactorily explained; experimental uncertainties may be particularly large in this case.

(23) A second *o*-substituent appears to retard the rate significantly; the rate enhancement factor decreases from 100 to 10 for the second *o*-methoxy substituent. Since steric interactions in a di-*o*-substituted *cis*-chalcone may be expected to affect the stabilization of charge exerted by the second substituent, it is believed that this apparent decrease in rate is due to the lessened electronic effectiveness of the second *o*-methoxy group.