

under reduced pressure to yield a colorless oil. Crystallization from acetone-water gave fine, white needles, 131 mg. (78%), m.p. 83–84°. An analytical sample melted at 84–85°,  $[\alpha]^{20D} -68.0 \pm 1^\circ$  (*c* 1.1).

*Anal.* Calcd. for  $C_{21}H_{34}O_2$ : C, 79.19; H, 10.76. Found: C, 79.44; H, 10.90.

**Stevic acid B, methyl ester (XXII)** was prepared in a manner similar to that described for XXI. From 300 mg. of XX was obtained 200 mg. (83%) of crystals from methanol; m.p. 105–115°. Three recrystallizations from dilute methanol gave white prisms, m.p. 118–120°,  $[\alpha]^{20D} -93.7 \pm 1^\circ$  (*c* 1.08).

*Anal.* Calcd. for  $C_{21}H_{34}O_2$ : C, 79.19; H, 10.76. Found: C, 79.42; H, 10.83.

**19-Hydroxystevane A (XXIII)** was prepared in a manner similar to that described for VII. From 131 mg. of methyl ester XXI was obtained a crude white solid, m.p. 147.5–153°, which on recrystallization from acetonitrile gave long, white needles, 87 mg. (73%), m.p. 153–154°,  $[\alpha]^{20D} -29.3 \pm 2^\circ$  (*c* 1.09).

*Anal.* Calcd. for  $C_{20}H_{34}O$ : C, 82.69; H, 11.80. Found: C, 82.55; H, 11.84.

**19-Hydroxystevane B (XXIV)** was prepared in a manner similar to that described for VII. From 200 mg. of stevic acid B, methyl ester (XXII) and 140 mg. of lithium aluminum hydride in refluxing tetrahydrofuran (6 hr.) was obtained 133 mg. (72%) of white solid, m.p. 133–136° (trans-crystallization at 125–130° from prisms to needles) from methanol. The resolidified compound melted at 142–144°,  $[\alpha]^{20D} -61.7^\circ \pm 2.2^\circ$  (*c* 0.87).

*Anal.* Calcd. for  $C_{20}H_{34}O$ : C, 82.69; H, 11.80. Found: C, 82.57; H, 11.82.

**19-Stevanal A (XXV)** was prepared in a manner similar to that described for IX. From 85 mg. of XXIII was obtained 76 mg. (90%) of white flakes, m.p. 109.5–118°. The crude compound was used immediately for thioacetal formation and no attempt was made to recrystallize it.

**19-Stevanol B (XXVI)** was prepared in a manner similar to that described for IX. From 174 mg. of XXIV was obtained 158

mg. of crude oil, used directly for the preparation of the thioacetal.

**19-Stevanal A, ethylene thioacetal (XXVII)** was prepared in a manner similar to that described for XI. From 76 mg. of crude aldehyde XXV was obtained 74 mg. of crude thioacetal by chromatography on 3 g. of grade II alumina (elution with petroleum ether, 30–60°). Attempts to crystallize this compound failed.

**19-Stevanal B, ethylene thioacetal (XXVIII)** was prepared in a manner similar to that described for XI. From 158 mg. of crude aldehyde XXVI was obtained 105 mg. (41%) of crystals, m.p. 128–134°. Recrystallization from ether-methanol raised the m.p. to 131–132.5°,  $[\alpha]^{20D} -75.4 \pm 3.2^\circ$ .

*Anal.* Calcd. for  $C_{22}H_{36}S_2$ : C, 72.46; H, 9.95. Found: C, 72.27; H, 10.15.

**Stevane A (XVII). Method 2.**—To a solution of 74 mg. of crude thioacetal XXVII in 40 ml. of dioxane was added 0.5 teaspoonful of Raney nickel and the mixture was refluxed for 18 hr. The catalyst was removed by filtration and the solvent removed under reduced pressure. The product was chromatographed on 1.8 g. of grade II alumina. Elution with petroleum ether (30–60°) gave a white solid, which on recrystallization from acetone gave 38.9 mg. of white needles (66%), m.p. 87.5–89°,  $[\alpha]^{20D} -30.3 \pm 1.5^\circ$  (*c* 1.09). A mixture m.p. with stevane A from method 1 showed no depression. Infrared and gas chromatographic retention times of both stevane A samples were identical.

**Stevane B (XVIII)** was prepared in a manner similar to that described for XVII (method 2). From 80 mg. of thioacetal XXVIII was obtained 25.6 mg. (42%) of white solid, m.p. 44.5–47°  $[\alpha]^{20D} -51.9 \pm 1.5^\circ$ . Recrystallization from acetone-methanol raised the m.p. to 53.5–55°,  $[\alpha]^{20D} -56.3 \pm 1.5^\circ$ . The compound was identical (mixture m.p., infrared spectra, gas chromatography) with stevane B from method 1. It was identical<sup>21</sup> with the hydrocarbon obtained from garryfoline<sup>14</sup> (gas chromatography, infrared spectra).

(21) We wish to thank Professor C. Djerassi for making these comparisons.

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## Keto-Enol Transformation of 1,2-Cyclohexanedione. I. Hydration and Keto-Enol Equilibria<sup>1-3</sup>

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Although 1,2-cyclohexanedione is normally available only as its mono enol, the ketone can be prepared in almost pure form through its bisulfite complex. The monohydrate of the ketone forms rapidly and almost completely in aqueous solution. Studies of the hydration reaction in aqueous dioxane at 25° lead to an equilibrium constant for hydrate formation of  $182 \pm 5$ . The keto-enol transformation is slow in aqueous solution but is catalyzed by both acids and bases. The stoichiometric concentration equilibrium constant,  $K_s = [K]/[E]$ , is close to unity in aqueous solutions which are dilute in both substrate and electrolyte but varies almost 10-fold from dilute acidic solutions to solutions which are 6 *M* in mineral acids. The explanation is shown to be that the activity coefficient of the ketone increases much more rapidly with electrolyte concentration than does that of the enol. Studies of the keto-enol equilibrium as a function of temperature lead, for formation of the ketone, to values of  $\Delta H^\circ = -6$  kcal./mole and  $\Delta S^\circ = -21$  e.u. This large entropy change is about the expected value for transformation of an unhydrated enol to a monohydrated ketone.

Only a few keto-enol equilibria have been studied in aqueous solution; most of these have been between  $\beta$ -diketones and their enols, a reason being that this is one important class of ketones for which significant amounts of enol are to be found in aqueous solutions.<sup>4-6</sup> Cyclic  $\alpha$ -diketones represent an interestingly different class of compounds to study. The cyclic character of these molecules can clearly contribute strain to the system and it is of interest to see the effect of this. A different but perhaps related reason is that cyclic  $\alpha$ -diketones tend to be strongly hydrated and this should have a large effect on the keto-enol equilibrium.

The present study considers both the hydration and keto-enol equilibria for a typical cyclic species, 1,2-cyclohexanedione. Although this compound is custom-

arily known only as its enol, Schwarzenbach and Wittwer some time ago presented data which indicated that it reached an equilibrium in aqueous solution in which the relative amounts of keto and enol were approximately one to one.<sup>7</sup> This result was uncertain in the sense that no direct evidence for the presence of ketone was obtained, but it did suggest the desirability of further studies of this system. Another incentive is the fact that closely related cyclic diketones have frequently been found to be hydrated. Thus it has been shown that one of the carbonyl groups of 3,3,6,6-tetramethyl-1,2-cyclohexanedione (a compound which cannot enolize) is almost completely hydrated.<sup>8</sup> Similarly, 3,4-diketotetrahydrofuran has been shown to be extensively hydrated.<sup>9</sup>

### Experimental

The mono-enol of 1,2-cyclohexanedione melts at about 38°. It forms colorless solutions in water and in anhydrous organic solvents such as chloroform and dioxane. It absorbs strongly in the ultraviolet, the main absorption being a broad peak with a

(1) Work supported by a grant from the Atomic Energy Commission.  
 (2) Presented in part at the 139th National Meeting of the American Chemical Society, St. Louis, Mo., April, 1961.  
 (3) Original data in thesis of Ronald Bakule, Cornell University, 1962, available from University Microfilms, Ann Arbor, Mich.  
 (4) For early references see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University, Ithaca, N. Y., 1953, p. 555.  
 (5) J. C. Reid and M. Calvin, *J. Am. Chem. Soc.*, **72**, 2948 (1950).  
 (6) J. Powling and H. J. Bernstein, *ibid.*, **73**, 4354 (1951).

(7) G. Schwarzenbach and C. Wittwer, *Helv. Chim. Acta*, **30**, 663 (1947).  
 (8) C. Sandris and G. Ourisson, *Bull. soc. chim. France*, 1524 (1958).  
 (9) E. C. Kendall and Z. G. Hajos, *J. Am. Chem. Soc.*, **82**, 3219 (1960).

maximum at 262  $m\mu$ , where the extinction coefficient is approximately 7000. This strong absorption permits convenient measurement of the concentration of enol in solution. The infrared spectrum of the anhydrous enol in chloroform is about as expected.

Direct preparation of the ketone tautomer is comparatively difficult, but it is possible to obtain it in fairly pure form by equilibration of the enol in aqueous solutions followed by separation of the two forms by utilization of their different solubilities in various extraction media. (The fact that this separation can be done at all indicates a slow rate of transformation of the two tautomers and the kinetic aspects of the reaction will be the basis of a later communication.) A more satisfactory preparation of the ketone is, however, the following. When a saturated solution of the mono-enol in water (approximately 10% by weight) is treated with an excess of a saturated solution of sodium bisulfite, the enol is transformed within a few hours into the bisulfite complex of the ketone. If the bisulfite complex is destroyed by acidification with strong acid, essentially pure ketone is produced. When this aqueous solution is extracted with chloroform and the latter solution is dried with magnesium sulfate, the solution exhibits the characteristic yellow-green color of cyclic  $\alpha$ -diketones. The ultraviolet spectrum of these solutions indicates, however, that even the better preparations of ketone are contaminated with from 3 to 5% of the enol form. Most studies of the ketone were in fact made with these slightly contaminated materials.

It was possible to prepare samples of the anhydrous ketone in an almost pure state by removing the chloroform under reduced pressure, but these materials had only a short life, apparently because of a strong tendency of the ketone to dimerize. As a consequence, the ketone was normally stored as a solution in an organic solvent. To study the ketone in aqueous solutions a relatively concentrated solution in dioxane was prepared by distillation of a chloroform solution under reduced pressure with concomitant addition of dioxane until the chloroform was removed. Aqueous solutions of the ketone were then prepared by addition of the dioxane solution to water. This led to the presence of small amounts of dioxane, but since the amount never exceeded 1% its effects were ignored.

Both the infrared and the visible spectra of the ketone are quite similar to spectra for previously reported substituted 1,2-cyclohexanediones.<sup>10,11</sup> In particular, in anhydrous solvents the ketone exhibits a characteristic absorption maximum at 412  $m\mu$ , with an extinction coefficient of about ten.

Studies of the keto-enol equilibrium were usually made with ketone and enol concentrations in the order of  $10^{-4}$   $M$ . The equilibrium enol content was determined by measurement of the ultraviolet absorption of the equilibrated solutions at 260  $m\mu$ . The ketone concentration at equilibrium was determined as the difference between the initial concentrations of ketone or enol and that of the enol at equilibrium. For most of the equilibrium studies the starting material was the mono-enol. However, in several experiments the starting material was the ketone and within experimental error identical values of equilibrium constants were obtained by the two procedures. All studies were made at constant temperature, the actual temperatures varying between 25 and 60°.

The analytical procedure used for experiments where the starting material was ketone necessitates accurate knowledge of the extinction coefficient of the enol both in dilute aqueous solution and in solutions of the catalyst acid. The necessary spectral data could usually be determined by direct measurement since the rate of transformation of the enol was sufficiently slow. However, in a few cases it was necessary to measure the optical absorption of solutions of the enol as a function of time and to extrapolate back to the time of mixing. As an example of the resulting data, the enol in water exhibits an extinction coefficient of  $6790 \pm 100$  at 260  $m\mu$ . In 7  $M$  perchloric acid the extinction coefficient was 6630 ( $\pm 100$ ), *i.e.*, there was no trend in  $\epsilon_{260}$  with changing acid concentration.

An obvious indication that the ketone is extensively hydrated in aqueous solution is that the characteristic diketone band at 412  $m\mu$  in dioxane disappears when water is added to the solution in dioxane and is also absent for solutions in pure water. As a consequence, the hydration equilibrium can only be studied in solutions of low water activity. The ultimate choice of solvent was an aqueous dioxane solution containing from 97 to 100% dioxane by volume. The total ketone concentration was normally of the order of  $10^{-2}$   $M$ . The actual concentration of the unhydrated ketone was determined by measuring the optical absorption of the solution at the 412  $m\mu$  wave length under the assumption that the extinction coefficient of the ketone is independent of the moderate changes in water-dioxane ratio. Concentration of the hydrated ketone was calculated as the difference between the total concentration and the observed value for the unhydrated ketone. The equilibrium constant was determined from the equation

$$K_N = [K \cdot H_2O] / [K_u] N_{H_2O}$$

where  $[K \cdot H_2O]$  is concentration of hydrated ketone,  $[K_u]$  is concentration of unhydrated ketone and  $N_{H_2O}$  is mole fraction of water. The reason for utilizing the mole fraction of water, rather than the water activity, in calculating the equilibrium constant was that in their extensive study of the hydration equilibrium of dichloroacetone in dioxane-water mixtures Bell and McDougall found considerably less medium effect for the constant when calculated in this way.<sup>12</sup> In the present case, equilibrium constants calculated with use of water activity are apparently also roughly constant, at a value of about 30, but the uncertainties about the actual values of  $a_{H_2O}$  for the concentration range involved<sup>13</sup> are so great as to make this alternate calculation procedure distinctly uncertain.

## Results and Discussion

Data on the hydration of the ketone in water-dioxane solutions at 25° are given in Table I. In the solvent mixtures considered here, and with the assumption that the extinction coefficient for the ketone at 412  $m\mu$  is independent of medium over the range considered, the equilibrium constant for hydration is found to be reasonably constant with a value of  $182 \pm 5$ . In view of the large extrapolation which is involved in going from these solutions to dilute aqueous solutions of the ketone, it is dangerous to assume that this equilibrium constant applies without change to solutions in water. However, it is notable that Bell and McDougall<sup>12</sup> found for the hydration of dichloroacetone that the mole fraction equilibrium constant was almost independent of medium for the solvent range of from 10 to 100% water in dioxane. In view of the extensive hydration of 1,2-cyclohexanedione in dioxane-water solutions and of the further fact that no observable absorption due to the 412  $m\mu$  band can be observed in the dilute aqueous solutions, it seems safe to conclude that the ketone is virtually entirely hydrated in aqueous media.

TABLE I  
HYDRATION OF 1,2-CYCLOHEXANEDIONE IN DIOXANE-WATER AT 25°

$N_{H_2O} \times 10^2$	$[K]/[K \cdot H_2O]$	$K_N$
0.155	3.39	190
.310	1.78	181
.465	1.16	186
.620	0.867	183
.774	.733	177
1.08	.517	179
1.55	.352	184
2.27	.239	184
3.02	.175	189
4.47	.124	180
7.72	.078	166
Average		$182 \pm 5$

A point of some importance is whether the hydration goes only to the monohydrate and we conclude that it does. Two points appear to bear on this conclusion. One is that there is no evidence from the equilibrium studies in mostly dioxane media for other than a simple equilibrium constant and this implies monohydration. An indirect but possibly more significant point is that analysis of the hydration phenomenon indicates that a principal reason for it is to relieve the strain which is a consequence of a cyclic  $\alpha$ -diketone structure. From consideration of molecular models, it appears that forming a monohydrate removes the strain rather completely. Furthermore, it appears that formation of the dihydrate would lead to steric crowding in the region of the oxygen functions.

An attempt was made to assess the extent of hydration of the single carbonyl group of the mono-enol and

(10) N. J. Leonard and P. M. Mader, *J. Am. Chem. Soc.*, **72**, 5388 (1950).

(11) C. Sandris and G. Ourisson, *Bull. soc. chim. France*, 958 (1956).

(12) R. P. Bell and A. O. McDougall, *Trans. Faraday Soc.*, **56**, 1281 (1960).

(13) J. R. Goates and R. J. Sullivan, *J. Phys. Chem.*, **62**, 188 (1958).

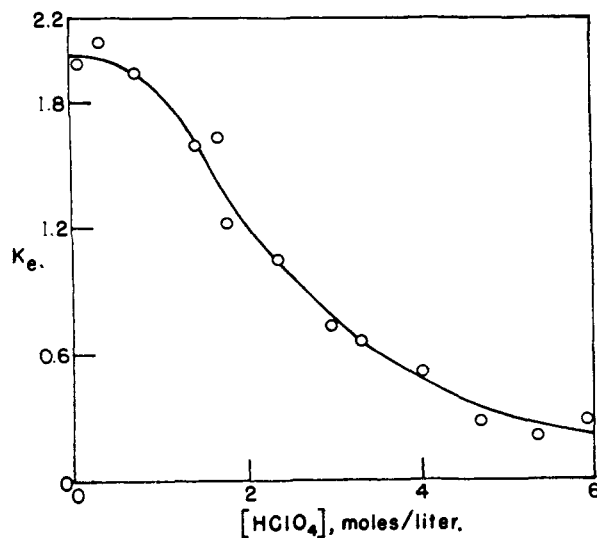


Fig. 1.—The concentration equilibrium constant,  $K_e = [K]/[E]$ , for the keto-enol equilibrium of 1,2-cyclohexanedione in aqueous solution at 25° as a function of concentration of perchloric acid.

no evidence for hydration could be found. Specifically, the extinction coefficient for the carbonyl group remains virtually unchanged in going from solutions of the enol in water to 75% dioxane by volume. We shall therefore assume that the enol is present in aqueous solutions in an unhydrated form.

The studies of the keto-enol equilibrium for 1,2-cyclohexanedione have been made in dilute aqueous solutions with strong acids as catalysts. A catalyst is necessary simply because the rate of transformation for this keto-enol system in water is otherwise extremely slow.<sup>14</sup> Using the symbol K for ketone in solution in all forms (hydrated and unhydrated) and the symbol E for the enol, we may define a concentration equilibrium constant  $K_e = [K]/[E]$  where [E] and [K] are total enol and total ketone concentrations, respectively. Figures 1 and 2 give plots of  $K_e$  as a function of concentration of strong acid catalyst for three catalysts, sulfuric, perchloric and hydrochloric acids. (In all cases the total concentration of ketone plus enol is in the order of  $10^{-4}$  M.) The graphs include points where equilibration started from the enol as well as points where equilibration started from the ketone and it is evident that there is no significant difference between the two sorts of experiments.

The most striking feature of the results in Fig. 1 and 2 is the marked dependence of the concentration equilibrium constant on concentration of electrolyte. The thermodynamic equilibrium constant,  $K_t$ , for this equilibrium is

$$K_t = \frac{a_K}{a_E} = \frac{[K]}{[E]} \times \frac{f_K}{f_E} = K_e \times \frac{f_K}{f_E}$$

where  $a$  denotes the activity of the given species and  $f$  the activity coefficient of the species, referred to the value of unity for a dilute aqueous solution. The clear implication of the large change in  $K_e$  with concentration of electrolyte is that the ratio  $f_K/f_E$  must increase by a factor of approximately eight in going from dilute solutions in pure water to solutions which are approximately 6 M in a strong acid. Since in a superficial sense the ketone and enol species are fairly

(14) As might be expected, basic species are considerably more effective catalysts than are acidic species and equilibrium may be reached relatively quickly with only small amounts of hydroxide ion as catalyst. However, no extensive use of basic catalysts has been made, partly because of our interest in the kinetics of acid catalysis, partly because there were some indications that side reactions occurred for solutions of the ketone in basic solvents.

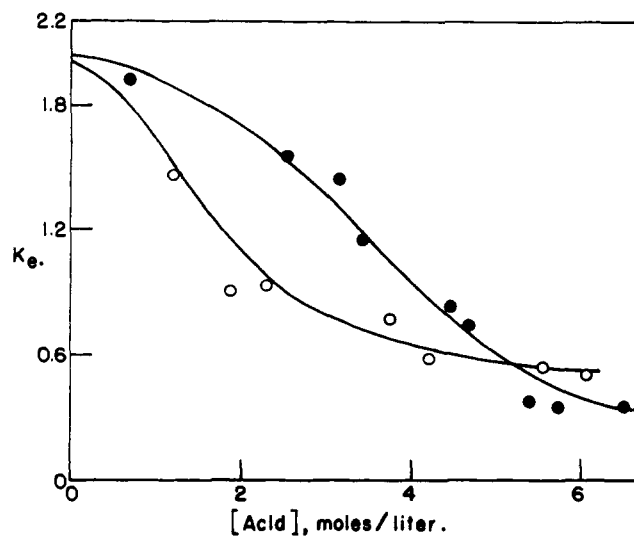


Fig. 2.— $K_e$  at 25° for the catalysts hydrochloric acid, data labeled O, and sulfuric acid, data labeled ●.

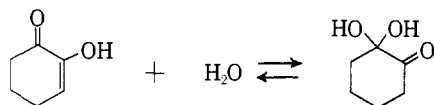
similar in size and in polar nature, it is important to establish that this large electrolyte effect is real.

To show this, we have made direct determinations of the influence of electrolytes on the activity coefficients of the two separate species, enol and ketone. It would, of course, be desirable to do this with the strong acid species themselves, but this is difficult in view of the catalytic nature. We have consequently attempted to choose an electrolyte whose salting in or salting out nature was similar to that of the mineral acids, the particular choice being sodium bromide.<sup>15</sup> Since solutions of this salt in water have virtually no catalytic activity for the keto-enol transformation, it is possible to study the equilibrium properties of the pure ketone and pure enol in aqueous solutions of the salt.

The procedure used for determining activity coefficients of the species was to measure their equilibrium partition between aqueous solutions of sodium bromide and the non-aqueous medium, chloroform.<sup>15</sup> All studies were made with ketone or enol concentrations in the order of *ca.* 0.02 M so that solutions in the organic medium can be considered to be nearly ideal. The result of these experiments is that sodium bromide causes marked salting out of the ketone species from water whereas it causes only slight salting out of the enol species. More specifically, for an aqueous solution of 6 M bromide,  $f_K = 13$  relative to the standard state value of unity for the infinitely dilute aqueous solution. For enol in the same salt solution,  $f_E = 1.8$ . Hence for a six molar solution of sodium bromide, the ratio  $f_K/f_E$  attains a value of about seven, compared to a value of unity for a salt-free aqueous solution. This increase is very close to that indicated for the mineral acids by the equilibrium studies of Fig. 1 and 2 and confirms the conclusion that in spite of their superficially similar nature the ketone and enol species are affected quite differently by electrolytes.

In seeking an explanation for these differences we turn to the fact that the ketone is very extensively hydrated in aqueous solutions. We should, in fact, really think of the keto-enol equilibrium as being between the monohydrated ketone and the unhydrated enol. Although from a kinetic standpoint the reaction is doubtless a step-wise one, the "main reaction" for transformation of the enol can be written

(15) F. A. Long and W. F. McDevitt, *Chem. Rev.*, **51**, 119 (1952).



In terms of the above equation, a possible reason for a change in the keto-enol equilibrium as a function of salt concentration is that the species water enters into the reaction. In going from dilute aqueous solution to six molar perchloric or sulfuric acid the activity of water drops by about a factor of about two and this should lead to a concomitant decrease in the concentration equilibrium constant. But since the total decrease in  $K_e$  is about a factor of eight, it is evident that an explanation based on changes in water activity alone is not sufficient. However, in view of the now somewhat different nature of the ketone species, *i.e.*, the fact that it is hydrated, it is perhaps not surprising that the activity coefficient for this species is differently affected by electrolytes than is that for the unhydrated enol.

The rather distinctive nature of this particular keto-enol equilibrium might be expected to show up in the thermodynamic parameters for the process and, to investigate this, studies of the temperature coefficient of the equilibrium constant have been made. The results are listed in Table II. The data are reasonably well fitted by the van't Hoff equation and, for the reaction of enol to give ketone, lead to a change in enthalpy of  $\Delta H^0 = -6 \pm 1$  kcal. per mole and an entropy change of  $\Delta S^0 = -21 \pm 3$  e.u.<sup>16</sup> The question

TABLE II

KETO-ENOL EQUILIBRIUM IN 1.75 M AQUEOUS PERCHLORIC ACID

$t$ , °C.	$K_e$	$t$ , °C.	$K_e$
25.0	1.21	47.4	0.54
25.0	1.22	53.1	.49
25.0	1.32	53.1	.51
25.0	1.50	53.2	.49
31.4	0.94	53.3	.46
31.4	.88	59.4	.40
31.4	.74	59.0	.41
39.7	.66	59.5	.43
40.4	.71		

(16) Data on the ketone-enol equilibrium for this system in solvent ethanol were reported some years ago for the two temperatures 25° and 50°<sup>17</sup> and it is of interest that the  $\Delta H^0$  and  $\Delta S^0$  values derivable from these data are in reasonable agreement with those for aqueous solutions. Specifically we calculate  $\Delta H^0 = -7$  kcal./mole and  $\Delta S^0 = -26$  e.u. from those results. The clear implication is that extensive alcoholation of the ketone occurs in the solvent ethanol.

(17) G. Hesse and G. Krehbeil, *Ann.*, **593**, 35 (1955).

now is, how do these values compare with the data for other keto-enol transformations?

One might quite reasonably expect the entropy changes for a keto-enol tautomerism in the gas phase to be close to zero and data which roughly support this were commented on some time ago by Conant and Thompson.<sup>18</sup> More recent studies of the equilibria for acetylactone and ethyl acetoacetate in a variety of solvents suggest that  $\Delta S^0$  is rather close to zero for all solvents, including water.<sup>4</sup> Nachod has experimental data for the first of these compounds in water and from these we calculate  $\Delta S_{298}^0 = -2.8$  e.u. for the reaction of enol to ketone in dilute aqueous solution.<sup>19</sup> Since there is no reason to expect either of these ketones to be significantly hydrated, it is reasonable to conclude that an uncomplicated keto-enol tautomerization will be characterized by a small entropy change in aqueous solution as well as in other solvents.<sup>20, 21</sup>

If, as in the present case, the keto-enol equilibrium is between a hydrated ketone and an unhydrated enol, one can expect that, owing to the loss of translational entropy for one mole of reactant, the value of  $\Delta S^0$  for the transformation of enol to ketone will be strongly negative. The implication is, of course, that the process of hydrating a ketone will in itself lead to a negative entropy term and this is demonstrated by the compilation of Bell and McDougall.<sup>12</sup> Their data show some variation with compound, but the average value of  $\Delta S_{298}^0$  for ketone hydration in aqueous solution appears to be about  $-18$  e.u. which is not far from the value predicted by translational entropy considerations alone. For formation of the very stable hydrates of formaldehyde and trichloroacetaldehyde the values are  $\Delta S_{298}^0 \approx -30$  e.u. We conclude that the observed  $\Delta S^0$  value of  $-21$  e.u. for the tautomerization of the enol of 1,2-cyclohexanedione is entirely consistent with the reaction equation given earlier and can be taken as evidence that the equilibrium being studied is indeed between a monohydrated ketone and an unhydrated enol.

(18) J. B. Conant and A. F. Thompson, Jr., *J. Am. Chem. Soc.*, **54**, 4039 (1932).

(19) F. C. Nachod, *Z. physik. Chem.*, **A182**, 193 (1938).

(20) Another relevant investigation of keto-enol equilibria in aqueous solution is that of Reid and Calvin<sup>5</sup> who studied compounds of the formula  $R-CO-CH_2-CO-CF_3$ . The average value of  $\Delta S_{298}^0$  was about zero for this group of ketones but the variations were large. This system is experimentally less tractable because of the very small enol contents at equilibrium. Hydration of the ketone is also more likely for these systems but appears not to have been investigated so far.

(21) For the enols of  $\beta$ -diketones in the gas phase one might expect some decrease in entropy for the hydrogen bonded form as compared to the open chain form. It is difficult, however, to assess the role of this for aqueous solutions where there is competition between internal hydrogen bonding and hydrogen bonding with the solvent.