luted with water and extracted with ether. From the extract was obtained 2 g. (4.3%) of a semi-solid yellow oil from which more 1,4-diphenylbutane separated.

Summary

Styrene treated with sodium and alcohol gives 75% of ethylbenzene and 25% of 1,4-diphenylbutane. This shows that polystyrene should be represented by formula II, in opposition to the heretofore accepted formula I. Only formula II is consistent with Mack's explanation of the rubber-like elastic properties of polystyrene.

COLUMBUS, OHIO RECEIVED JULY 15, 1936

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NEW HAMPSHIRE]

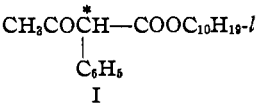
A Comparison of the Rate of Racemization with the Rate of Enolization

BY R. H. KIMBALL

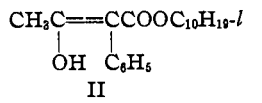
It has long been assumed that optically active ketones, esters and acids can undergo racemization through formation of the inactive enol, which reverts to the racemic mixture. General acceptance of this mechanism has followed recognition of the fact that such substances can only be racemized when they are capable of enolization. This has been confirmed recently by Conant and Carlson,[1] who conclude that the rate of racemization can be considered as the rate of enolization, and point out the significant fact that whatever mechanism is assumed the rate of enolization cannot be faster than that of racemization, since the enol is necessarily inactive.

Whether enolization can be *slower* than racemization can only be determined by measuring the loss of optical activity and the development of enol simultaneously by independent methods. The familiar Kurt Meyer method of bromine titration has been applied in the past to measurement of the rate of enolization of acetoacetic ester and related substances.[2] An unsuccessful attempt to combine this method with polarimetric measurements has been described by Wren,[3] who tried to follow the development of enol during the racemization of methyl phenyl succinate by bromine titration, but failed because no detectable amount of enol was present. The difficulty has been that substances appreciably enolized racemize so easily that they cannot be obtained optically active; while substances which can be obtained optically active are not perceptibly enolized.

The substance employed in the present attack on the problem is the menthyl ester of α-phenylacetoacetic acid[4] I.



I



II

The form of this substance obtained by crystallization from methyl alcohol is the ketonic modification, as demonstrated by the fact that the fresh solution gives no color with ferric chloride and does not absorb bromine.

Freshly dissolved in benzene or alcohol the substance is dextrorotatory. The rotation at once starts to decrease, passing through zero and finally reaching a constant strongly levo value. This takes weeks without a catalyst, but addition of a small amount of piperidine or barium hydroxide brings it to equilibrium in a few minutes.

Rupe[4] interpreted this to mean that the active menthol has brought about resolution of the α-phenylacetoacetic acid, the form crystallizing from methyl alcohol being the dextro-keto modification I because of its dextro rotation—a long series of similar menthyl esters in which resolution is not possible being strongly levorotatory like menthol itself. He ascribed the mutarotation to formation of the enol II in which the optical activity of the alpha carbon atom is lost. Since only one of the three asymmetric carbon atoms is affected, this is not a true but a partial racemization, and at equilibrium the solution will contain the enol mixed with the diameric dextro-keto and levo-keto modifications.

In the usual true or partial racemization the proportion of enol is always negligible. Here on the contrary the enol steadily increases during the mutarotation until it constitutes the major part of the equilibrium mixture. The most significant comparison between the rate of this development of enol and the rate of racemization of the carbon atom involved will be made during

(1) Conant and Carlson, THIS JOURNAL, **54**, 4048 (1932).

(2) K. H. Meyer, *Ann.*, **380**, 233 (1911); *Ber.*, **44**, 2725, 2729 (1911); Grossman, *Z. physik. Chem.*, **109**, 305 (1924).

(3) Wren, *J. Chem. Soc.*, **113**, 210 (1918).

(4) Rupe, *Ann.*, **395**, 91 (1913); **398**, 372 (1913).

the early stages of the reaction, when the reverse processes are not yet apparent and the change of *d*-keto to enol is the only thing taking place.

With this in view the solvent chosen was cyclohexane, in which enolization is 71% complete at equilibrium. About 10 g. of pure crystalline *d*-keto form was weighed into a volumetric flask and made up to 100 cc. with pure cyclohexane containing a few parts per million of piperidine as the catalyst. The solution was quickly transferred to an all-glass polarimeter tube with an attached chamber, water-jacketed to maintain constant temperature and designed to permit frequent and thorough mixing of the solution (Fig. 1). Polarimeter readings were taken at intervals through the first half of the racemization.

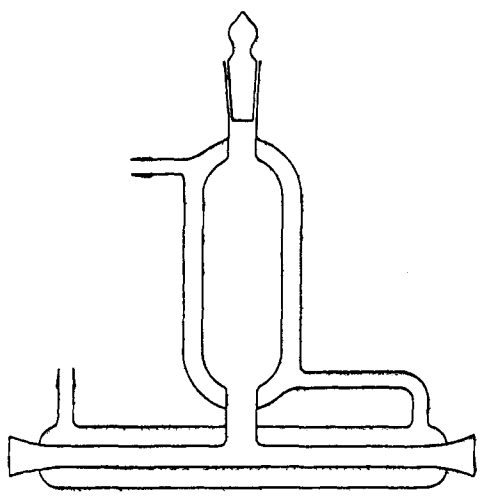


Fig. 1.—Polarimeter tube.

The development of enol was followed by pipetting out samples of the solution and titrating them with dilute alcoholic bromine to the first bromine color, the "direct" method of Kurt Meyer. Here it proved very satisfactory since the bromine was absorbed rapidly in the cold, and the sharp end-point persisted for five minutes. Finally more catalyst was added and the reaction was allowed to run to equilibrium, to obtain the values for the rotation and for the concentration of enol.

The pseudo-unimolecular velocity constant $k_1 + k_2$ for the racemization was obtained in the ordinary way by plotting the values of log $(\alpha_t - \alpha_{eq.})$ against t, where α_t and $\alpha_{eq.}$ represent the polarimeter readings at time t and at equilibrium. For the enolization the volume of thiosulfate used by each sample is proportional to the concentration of enol, so that log $(V_{eq.} - V_t)$ was plotted against t. The best straight lines were run through these points and $k_1 + k_2$ calculated from the slope in the usual manner. For both the racemization and the enolization the points fell closely along straight lines (Fig. 2, A and B) and the reactions therefore follow the unimolecular law. Measurements normally extended over a period covering the first half of the racemization and the first quarter of the enolization, in one case the racemization being followed to 80% completion and the enolization to 50% completion without the appearance of a trend.

The data for three runs with varying amounts of catalyst are summarized in Table I.

TABLE I

VELOCITY CONSTANTS × 10^4 TIME IN MINUTES FOR THE RACEMIZATION AND ENOLIZATION OF MENTHYL α-PHENYLACETOACETATE I

Run no.	I	II	III
Approx. concn. piperidine in parts per million	8	10	12
$k_1 + k_2$ for racemization	12.8	17.8	24.8
$k_1 + k_2$ for enolization	3.72	6.64	8.02
k_1 for enol. (graphically)	2.51	4.48	6.17
k_1 for enol. (calculated)	2.59	4.71	6.34
k_1 polarimetrically using α_{enol}	14.5	20.1	28.5
k_r (total racemization)	8.22	16.3	21.6
k_{dl} (racem. through ion)	5.47	10.5	14.3
k_e (racem. through enol)	2.75	5.80	7.32
Ratio k_{dl}/k_e	1.99	1.82	1.95

It is evident that racemization as measured by $k_1 + k_2$ proceeds several times as fast as enolization. However, a much more significant comparison can be made. If the *d*-keto form loses its activity through changing directly to the enol, the rate of this change k_1 can be obtained from data taken in the early stages of the reaction, and it should have the same value by both methods of measurement.

For the enolization k_1 is easily determined by plotting the log of the concentration of keto against t in the usual way. The points still fall on a straight line through the measured range (Fig. 2, D) and the slope of this line gives the values of k_1 for enolization shown in Table I.

It is also possible to calculate k_1 from the two equations for $k_1 + k_2$ and for the equilibrium constant in the usual way, and the values are in satisfactory agreement.

To measure the rate of change of *d*-keto to enol polarimetrically, it is necessary to know the rotatory power of the pure enol. Attempts to isolate the enol by chemical methods failed, shift to the equilibrium mixture taking place too easily.

Distillation under a high vacuum from a Hickman molecular still was finally successfully employed. The crystalline keto form was catalyzed with a little barium hydroxide and distilled slowly, yielding a uniform distillate containing 64% of enol, which probably represents the equilibrium in the vapor phase.[5] This mixture was repeatedly fractionated in the absence of catalyst, the distillate becoming progressively richer in enol until the concentration reached 93.8%, which apparently represents a constant boiling mixture. This is a colorless viscous oil, hardening to a glass at low temperatures without crystallization; it has the same composition as the ketonic form, gives an immediate deep purple color with ferric chloride, and absorbs bromine rapidly in the cold. Alone or in solution it is very stable in the absence of catalyst, but with a trace of piperidine it undergoes mutarotation to the same equilibrium mixture reached by the *d*-keto form.

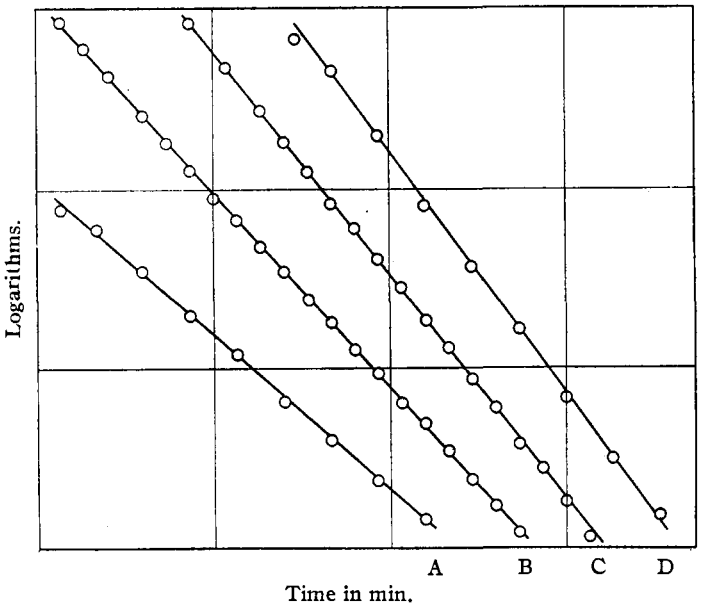


Fig. 2.—Graph of run III: A, $k_1 + k_2$ for enolization ($\times 10^4$) = 8.02; B, $k_1 + k_2$ for racemization = 24.8; C, k_1 polarimetrically using α_{enol} = 28.5; D, k_1 for enolization (titrimetrically) = 6.17. Range of measurement: A and D 3–18% enol; B and C 7–65% racemization. Time scale: unit square = 150 min. Logarithm scale: unit square for A = 0.0600; for B and C = 0.1500; for D = 0.0300.

The value for the rotation of pure enol was obtained by following this mutarotation in cyclohexane by the polarimeter and by titration in the usual way. On plotting this series of values for decreasing enol content against the rotation, a nearly straight line was obtained and extrapolated to the rotation of pure enol as shown in Fig. 3. The accuracy of this extrapolation is favored by the small change in rotation, and the value obtained $[\alpha]^{25}D$ −56.5° should be close to the true rotation of the enol.

The rate of change of *d*-keto to enol can now be determined polarimetrically by substituting α_{enol} for $\alpha_{eq.}$ and plotting log $(\alpha_t - \alpha_{enol})$ against t (Fig. 2, C). The points still fall along a straight line through the first half of the racemization, and the slope of this line gives values for k_1 (Table I) which are four or five times as large as the values of k_1 for the same change of *d*-keto to enol obtained by titration.

There seems to be no doubt therefore that in this substance the alpha carbon atom loses its optical activity much faster than the enol is produced. This can hardly be explained by some means of racemization operating independently of the enolization, in view of the almost inseparable connection between the two processes.[6] As the only alternative it is evident that *enolization cannot consist of a simple reversible change of keto to enol, but must proceed through some intermediate step.* In this intermediate step the configuration of the alpha carbon atom is destroyed, and since only part of the active substance changing to the intermediate in a given time goes on to form enol, and part reverts to *inactive* keto, the rate of racemization will be faster than the rate of enolization.

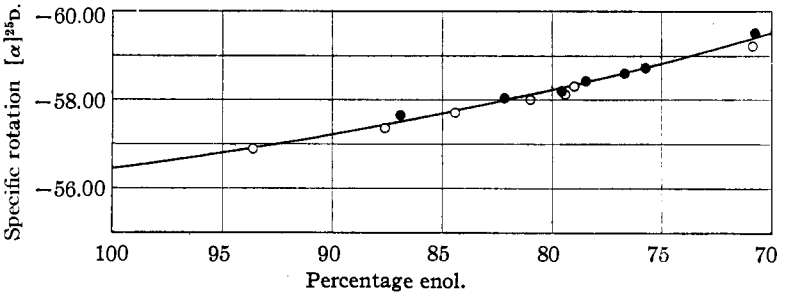


Fig. 3.—Mutarotation of constant boiling mixture extrapolated to 100% enol to obtain $[\alpha]^{25}D$ − 56.5°: ○, run I; ●, run II.

(5) Conant and Thompson, THIS JOURNAL, **54**, 4039 (1932).

(6) Conant and Carlson, THIS JOURNAL, **54**, 4048 (1932); discussion by Wagner-Jauregg in "Stereochemie," ed. Freudenberg, Franz Deuticke, Vienna, 1933, p. 858.

The relationship between racemization and enolization from the standpoint of the ionic theory of prototropic change has been discussed recently by Ingold and collaborators[7] in several papers which appeared during the course of this work. They formulate the mechanism of keto–enol tautomerism under the influence of a basic catalyst in the usual way[8]

$$B + H{-}C{-}C{=}O \rightleftharpoons BH + [C{-}C{=}O]^- \rightleftharpoons B + C{=}C{-}OH$$

and point out that if the configuration of the alpha carbon atom is retained in the common ion, the rate of enolization and of racemization should be equal; on the other hand, if the asymmetry is lost in the common ion, the rate of racemization must exceed that of enolization.

They tested the question in the methyleneazomethine system

$$C(H){-}N{=}C \rightleftharpoons C{=}N{-}C(H)$$

by comparing the rate of racemization of an active tautomeride under the influence of sodium ethoxide with the rate of its isomerization as determined by chemical analysis. In three cases the rates were identical within the experimental error, and the authors conclude that in this system the intermediate anion does not attain kinetic freedom and therefore retains its optical activity up to the instant of transformation into the inactive isomer.

In the base-catalyzed keto–enol system now under consideration the racemization takes place much faster than the formation of enol; and some intermediate stage in the process unavoidably must be recognized. If the ionic mechanism is adopted it follows that contrary to the situation in the methyleneazomethine system the intermediate anion does not retain its asymmetry, so that recombination with the proton gives both enol and *racemized* keto forms and accounts for the higher rate of racemization.

The existence of some supplementary means of racemization apart from conversion to the enol makes it obvious that the values of k_1 so far obtained do not express the true rate of racemization nor its relationship to the rate of enolization. Both can be calculated, however, from the data at hand as follows.

(7) Ingold and Wilson, *J. Chem. Soc.*, 93, 773 (1934); Hsû, Ingold and Wilson, *ibid.*, 1778 (1935); Hsû and Wilson, *ibid.*, 623 (1936).

(8) *Cf.* Bartlett, THIS JOURNAL, **56**, 969 (1934); Watson, Nathan and Laurie, *J. Chem. Phys.*, **3**, 170 (1935); Watson and Yates, *J. Chem. Soc.*, 1208 (1932); Pedersen, *J. Phys. Chem.*, **38**, 619 (1934).

Adopting some form of intermediate as necessary to acount for the results, the racemization of the menthyl ester is represented by scheme (1), where D, L, E and B represent, respectively, the *d*-keto form, the *l*-keto form, the enol and the intermediate, presumably the common anion. In the ordinary partial racemization such as the inversion of menthone where the amount of E is always imperceptible, the measured "rate of racemization" is simply the rate at which the original rotation of D changes to the rotation of the equilibrium mixture DL. As each molecule of D reacts it becomes part of the equilibrium mixture, so we can consider the *original* active substance D* as changing *irreversibly* to DL at a rate k_r equal to the measured rate of racemization.

$$\begin{array}{ccccc} & & B & & \\ & \overset{k_3}{\swarrow}\uparrow\overset{k_4}{\searrow} & \downarrow k_5 & \overset{k_4}{\swarrow}\uparrow\overset{k_3}{\searrow} & \\ D & \overset{k_1}{\rightleftharpoons} & B & \overset{k_2}{\rightleftharpoons} & L \\ & & \downarrow k_5 & & \\ & & E & & \end{array} \qquad (1)$$

$$\begin{array}{ccccc} & & B & & \\ & & \downarrow k_5 & & \\ D^* & \xrightarrow{k_r} & B & \xrightarrow{k_3 + k_4} & DL \\ & & \downarrow k_5 & & \\ & & E & & \end{array} \qquad (2)$$

$$\begin{array}{ccc} & \overset{k_{dl}}{\nearrow} & DL \\ D^* & & \\ & \underset{k_e}{\searrow} & E \end{array} \qquad (3)$$

$$k_{dl} + k_e = \frac{2.3}{t} \log \frac{C_{0D^*}}{C_{D^*}} \qquad (4)$$

$$\frac{k_{dl}}{k_e} = \frac{C_{DL}}{C_E} \qquad (5)$$

Representing the case at hand in the same way reduces (1) to (2), for early stages of the reaction where k_6 can be neglected. And since B changes immediately to DL and to E as fast as it is produced from D*, the effect is that of a direct change of D* simultaneously to DL and to E as shown in (3), where $k_{dl} + k_e = k_r$ the total rate of racemization, and $k_{dl}/k_e = (k_3 + k_4)/k_5$. The individual rates can now be obtained from equations (4) and (5), where C_{0D^*}, is the concentration of D* at t_0 and C_{D^*}, C_{DL} and C_E are the concentrations of D*, DL and E at any given time t.

In order to calculate these concentrations it is necessary to know the specific rotation of each substance. $[\alpha]_{D^*}$ and $[\alpha]E$ are already known and $[\alpha]DL$ can be obtained from the composition and rotation of the equilibrium mixture of DL and E resulting from complete racemization. From first principles it is apparent that in system (1) the *relative* proportions of D and L at equilibrium are independent of the presence or amount

of E or of the mechanism involved. The same mixture of D and L would result if E were negligibly small as in the ordinary partial racemization; therefore it corresponds exactly to the DL of schemes (2) and (3). Making the usual assumption that the rotations are additive in these dilute solutions, and knowing $[\alpha]$E and the concentrations of E and DL in the equilibrium mixture, $[\alpha]$DL can be obtained by difference. In the three runs $[\alpha]DL = -67.4, -67.8$ and $-68.5°$, respectively, the individual values being used in each case. For the others the values $[\alpha]E = -56.5°$ and $[\alpha]D^* = -15.8°$ (average) were employed.

The next step toward applying equations (4) and (5) is the calculation of C_{D^*}, C_{DL} and C_E at time t, which will be illustrated for run III. Here $C_{0D^*} = 10.584$ (g. in 100 cc. of solution), t_0 = time when d-keto was put into solution, and t was chosen as three hundred and fifty minutes, close to the half time of racemization. From the straight lines plotted for $k_1 + k_2$ of racemization and of enolization (B and A, Fig. 2) were read off the correct values for the rotation ($\alpha D^* + \alpha DL + \alpha E = -10.30°$) and for the concentration of enol ($C_E = 1.903$ g.) at time t. Subtracting C_E from the total concentration 10.584 g. gives equation (6).

$$C_{D^*} + C_{DL} = 8.681 \text{ g.} \quad (6)$$

$$0.3707\ C_{D^*} + 1.603\ C_{DL} = 7.79° \quad (7)$$

Subtracting the rotation of 1.903 g. of enol (αE) from $-10.30°$ gives $\alpha D^* + \alpha DL = -7.79°$, which by the use of $[\alpha]D^*$ and $[\alpha]$DL can be expressed as equation (7). Solving these two equations we now have $C_{0D^*} = 10.584$, $C_{D^*} = 4.972$, $C_{DL} = 3.709$, $C_E = 1.903$, and $t = 350$. Substituting these values in equations (4) and (5) and solving, $k_r = k_{dl} + k_e = 21.6$, $k_{dl} = 14.3$, and $k_e = 7.3(\times 10^{-4})$. The values obtained in the same way for runs I and II are shown in Table I, together with the ratios of k_{dl} to k_e which are close to 2 : 1 and check satisfactorily. From the previous discussion it is evident that k_r is comparable to the rate measured in the ordinary partial racemization; k_{dl} represents the fraction of this racemization (around two-thirds) taking place through the common ion without involving the enol; and k_e the fraction (around one-third) involving actual transformation to the enol.

It seems quite probable that racemization may take place in a similar way in ordinary ketones where no detectable enol ever appears. The fact that only part of the racemization can be ascribed to "enolization" in the usual sense of the word calls into question the validity of the familiar principle that the rate of racemization can be considered as the rate of enolization. The ability of a substance to ionize and the stability of the configuration of the common ion may be the important factors governing its racemization, rather than the actual formation of molecular enol.

The other reaction of ketones commonly regarded as a measure of enolization is halogenation in the α-position to the carbonyl group.[7-9] Recent comparisons have shown that the rate of halogenation and the rate of racemization of optically active ketones are substantially equal both in the presence of acids and of bases,[10] and the suggestion has been made that the halogen actually adds to the intermediate ion, at a rate equivalent to the rate of ionization. Since it now appears that under basic catalysis ionization alone can result in racemization, the rate of halogen absorption may be a measure of racemization (k_r) but not of enolization (k_e) in the sense of actual formation of molecular enol. The more "saturated" character of the intermediate ions or salt-like complexes generally postulated in acid catalysis[7,8,10] would seem to favor a more stable configuration. Rate measurements now being made of the racemization and enolization of the menthyl ester in the presence of acids may serve as a test of this question.

In another respect, however, the present results are difficult to interpret by the ionic theory of prototropic change. On general grounds Ingold and his collaborators[7] have concluded that in basic catalysis the reversible change from anion to enol must be very much faster than that from keto to anion, so that the observed rate of racemization should be substantially equal to the rate of enolization. The same opinion has been expressed by Pedersen[8] from the fact that rapid addition of a hydrochloric acid–bromine water mixture to an alkaline solution of acetoacetic ester indicated complete transformation of the anion to the enol.

In the case at hand, however, the anion apparently reverts to the keto form twice as fast as

(9) Bartlett and co-workers, THIS JOURNAL, **55**, 4992 (1933); **56**, 967 (1934); **57**, 1596, 2580 (1935); Watson and co-workers, *J. Chem. Soc.*, 217, 220, 890 (1933); 3318 (1931); Watson, *Chem. Rev.*, **7**, 173 (1930), includes a review of the literature.

(10) Bartlett and Stauffer, THIS JOURNAL, **57**, 2580 (1935); Ingold and Wilson, *J. Chem. Soc.*, 773 (1934); Hsü and Wilson, *ibid.*, 623 (1936).

it goes on to the enol. In scheme (1) k_5 is less than $k_3 + k_4$, but the amount of enol at equilibrium is greater than the amount of keto; it follows that $k_1 + k_2$ is greater than k_5, or the *keto form ionizes more rapidly than the enol.* This surprising result may perhaps be explained by the fact that enols of this type probably have a chelated structure, in which the mobility of the hydrogen may be reduced even below that in the ketonic form.

These considerations point to an alternative explanation of the observed difference between the rate of racemization and the rate of enolization of the menthyl ester. We may be dealing with a rapid and highly reversible shift to a small amount of open-chain enol which governs the racemization, followed by a slower accumulation of chelated enol which determines the rate measured by titration. It is hoped that further studies now in progress may aid in answering this and related questions.

Experimental

Acetobenzyl Cyanide, $CH_3COCH(C_6H_5)CN$.—Reagents must be pure and free from water and acids. Ethyl alcohol was dried twice over quicklime. Ethyl acetate was washed and fractionated from phosphorus pentoxide collecting over 0.5° range. Benzyl cyanide was freshly distilled at ordinary pressure and collected over 1.5° range.

Sixty-nine grams (3 moles) of sodium is dissolved in 870 cc. of dry alcohol, and a mixture of 351 g. (3 moles) of benzyl cyanide and 264 g. (3 moles) of ethyl acetate added, the mixture refluxed for an hour and allowed to stand overnight. The solid sodium derivative is quickly dissolved by adding 1.5–2 liters of water at 25°, and cracked ice added to keep the solution ice cold. It is washed with ether and air drawn through the solution under a partial vacuum till free from ether. A cold mixture of 195 cc. of acetic acid and 600 cc. of water is added slowly with shaking and the precipitated acetobenzyl cyanide filtered off and washed. It is purified by dissolving in 800 cc. of hot methyl alcohol, boiling with Norit if necessary, diluting with warm water and cooling; yield 300–310 g. (63–65%) of colorless material m. p. 88.5–89.5°.

Alpha-Phenylacetoacetic Ester, $CH_3COCH(C_6H_5)COOC_2H_5$.—The low yields of the previous methods[4,11] are avoided by hydrolyzing the imido ester in aqueous acid where the insolubility of the product protects it from decomposition.

A solution of 159 g. (1 mole) of acetobenzyl cyanide in 403 cc. of dry alcohol is saturated in the cold with carefully dried hydrogen chloride. After five to eight hours saturation is complete and the flask is allowed to stand overnight at room temperature with occasional shaking for the first hour.

Excess hydrogen chloride is removed by adding boiling chips and evacuating the flask in a water-bath at 40°. Two hundred grams of sodium carbonate is dissolved in 1200 cc. of water and ice added. Into this the reaction mixture is poured with vigorous shaking, the liberated imido ester extracted at once with generous portions of ether, and the ether washed well to remove alcohol.

The imido ester is extracted from the ether and hydrolyzed as follows: 100 g. of 98% C. P. sulfuric acid is poured into 700 cc. of water, and excess ice stirred in. The ether is shaken with cracked ice till cold, and the water separated. About one-half of the ice-cold acid is added, shaken vigorously for exactly fifteen seconds[12] and drawn off at once. The operation is repeated with the remaining acid in two portions. The ether is washed with sodium bicarbonate and dried over sodium sulfate, and yields 20–30 g. of crude α-phenylacetoacetic ester on distillation.

The solution of imido ester sulfate quickly turns cloudy from hydrolysis to the product. This is completed by heating on the steam-bath to 50° for one-half hour, separating the ester and reheating the aqueous layer vigorously for forty-five minutes. Extraction with ether and fractional distillation *in vacuo* yields 103–167 g. (50–81%), b. p. 139–143° (12 mm.).

Menthyl α-Phenylacetoacetate, I.—A mixture of 100 g. of α-phenylacetoacetic ester (freshly distilled) and 94 g. of *l*-menthol (E. K. Co., C. P.) in a 250-cc. modified Claisen flask with a wide side-arm is heated to 150–160° (thermometer in the mixture) for three hours.[4] The excess menthol is removed on the water pump and the menthyl ester distilled on the oil pump between 140–155° (0.5 mm.). From this mixture rich in enol the *d*-keto form is obtained by the asymmetric isomerization which takes place on slow evaporation of a methyl alcohol solution of the oil from an open dish at room temperature, adding alcohol at intervals to maintain a crystalline mush which favors the separation of the less soluble *d*-keto form. After a week or more the accumulated solid is purified by rapid recrystallization five or six times from pure methyl alcohol. The filtrates evaporated slowly in the same way yield a larger crop of pure product, and the process can be continued till most of the material is obtained as the pure *d*-keto form.

Menthyl α-phenylacetoacetate I crystallizes in long colorless prisms melting not quite sharply at 77–78.3° in Pyrex capillary tubes (67–76° in soft glass—Rupe[4] gives 69°). A fresh solution does not absorb bromine and gives no color with ferric chloride, slowly turning deep purple as enolization sets in. It is not completely stable and was always recrystallized shortly before use.

Contrary to Rupe[4] the substance is dextrorotatory in alcohol. Since his alcoholic solution gave an immediate color with ferric chloride it was doubtless partially racemized. This or the use of soft glass melting point tubes may also explain the lower melting point (69°) reported by him. Other constants check satisfactorily.

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.9; H, 8.9. Found: C, 76.0, 76.2; H, 8.8, 8.6. Specific rotation in cyclohexane $[\alpha]^{25}D$ −15.84°, mutarotating to $[\alpha]^{25}D$ −59.83°; $[\alpha]^{25}_{5461}$ −19.0°; in methyl alcohol $[\alpha]^{25}_{5461}$ +21.9°.

(11) Beckh, *Ber.*, **31**, 3160 (1898); Post and Michalek, THIS JOURNAL, **52**, 4359 (1930); Conant and Thompson, *ibid.*, **54**, 4039 (1932); A. F. Thompson, Dissertation, Harvard University, 1932; Bodroux, *Compt. rend.*, **151**, 235 (1910); *Bull. soc. chim.*, [4] **7**, 851 (1910); Walther and Schickler, *J. prakt. Chem.*, [2] **55**, 343 (1897).

(12) Any delay results in hydrolysis of some of the imido ester to the product, which stays in the ether layer.

Per cent. enol at equilibrium: liquid equil. mixt. ord. *t.* 40.0; 5% in methyl alcohol 21.5; 10% in ethyl alcohol 33.3; 10% in benzene 49.2; 10% in cyclohexane 71.0; 4% in petroleum ether 73.8. Effect of concn. on % enol in cyclohexane:

Concn., %	20	10	3.5	1.75	0.87
Enol, %	64.7	71.0	72.8	73.2	73.9

Enolic Form of Menthyl α-Phenylacetoacetate, II.—The pure *d*-keto form racemized quickly at 100° but only slowly at 80°. Since it could not be distilled below 135° by ordinary methods, high vacuum distillation was employed, using a butyl phthalate condensation pump[13] and Hickman high vacuum still (Fisher model) heated by a small metal bath with a tall closed can between dish and flame for even temperature control. In general about 50–60 g. of pure *d*-keto form was catalyzed with a pinch of barium hydroxide and distilled slowly at 85–95°, coming over as a colorless oil with a uniform enol content of 64%. This was redistilled in two portions without catalyst and the first half or two-thirds collected and redistilled in the same way. The temperatures varied from 75–85° (bath temp.) at 2–6 × 10^{-4} mm. pressure. As the fractions became too small they were combined with others of the same grade from additional runs. Four or five fractionations increased the enol content to 92–94%, the highest which could be reached by distillation. Repeated attempts failed to increase this by fractionation under the most favorable conditions; for example, 12 g. containing 93.4% enol was distilled and the first 3.5 g. collected contained 93.8% enol. That this was not the result of ketonization during distillation but shows the presence of a constant boiling mixture of keto and enol was confirmed by distilling 23 g. containing 92% enol and separating it into six fractions which contained, respectively, 93, 90, 94, 93, 89 and 75% of enol. The proportion of enol in the distillate was therefore constant until two-thirds of the material had distilled over, and the effect of ketonization only became apparent in the last two fractions.

This constant boiling mixture contains 93.8% enol as the average of fourteen preparations. It is a colorless viscous oil, hardening to a glass at low temperatures, and is isomeric with the ketonic form.

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.9; H, 8.9. Found: C, 75.7; H, 8.8.

Fresh solutions give an immediate deep purple color with ferric chloride and absorb bromine rapidly in the cold. It is quite stable in the absence of catalyst, showing little or no decrease in enol content after two weeks in the refrigerator. A 10% solution in cyclohexane showed a constant rotation $[\alpha]^{25}D$ −56.9° for an hour but on the addition of a trace of piperidine it mutarotated to the same equilibrium mixture reached by the keto form: from enol $[\alpha]^{25}D$ −59.2°, −59.5°; 70.9, 70.7% enol; from keto $[\alpha]^{25}D$ −59.8°; 71.0% enol.

The specific rotation of pure enol was obtained by following the mutarotation in cyclohexane polarimetrically and by titration exactly as described below for the ketonic form. In run I the catalyst was added after the first point (Fig. 3) had been obtained. In run II the catalyst was mixed with the solvent as customary with the keto form and mutarotation had proceeded somewhat before the first reading.

Purification of Materials. Methyl Alcohol.—C. P. absolute acetone-free methanol was distilled three times through an all-glass Pyrex apparatus with a 6-ball Snyder column rejecting about one-third. This was used in the titrations and all apparatus was rinsed with it just before use and dried in a current of air or by evacuation.

Cyclohexane.—E. K. Co. Pract. was treated to remove benzene,[14] washed with potassium hydroxide solution, dried and distilled through the all-glass fractionating apparatus, then a second time over potassium hydroxide and twice alone and obtained constant boiling. In this solvent mutarotation was so slow as to be insignificant compared to the catalytically induced rates.

Piperidine.—The unsaturates present in commercial C. P. piperidine were removed by differential oxidation of nitrosopiperidine[15] and fractionation from potassium hydroxide, yielding material boiling at 105.4–105.7° and stable toward permanganate. The amount used was regulated by adding small drops of a 1:100 solution in cyclohexane.

Rate Measurements.—From 10.0–10.6 g. of freshly recrystallized menthyl ester was weighed into a 100-cc. Pyrex volumetric flask and made up to volume with cyclohexane containing the piperidine catalyst. The solution was quickly transferred to the polarimeter tube (Fig. 1) and reading started, using a Franz Schmidt & Haensch half shade polarimeter read to 0.01° and a G. E. Sodium Lab-Arc. The temperature was held at 25 ± 0.1° by circulating water from the thermostat through the polarimeter tube jacket. The total change of rotation in the 2.340-dm. tube was 10.5° and some 20–30 readings were taken in the range between 7–15 and 50–65% racemization.

The enolization was followed over the same period. At intervals the solution was shaken and 5 cc. removed with a Pyrex pipet, run into 13 cc. of ice-cold methyl alcohol, and titrated with fresh methyl alcoholic bromine of such strength that 10–20 cc. was required. Bromine was absorbed instantly and was added to the first bromine color. The end-point was sharp and persisted for five minutes, and could be restored for an equal time by an additional drop or two of bromine. A correction was applied for the excess of bromine by subtracting the amount needed to bring an equal volume of methyl alcohol to the same color. This corrected volume was run into double the equivalent amount of 0.2 *N* potassium iodide and titrated with standard 0.05 *N* thiosulfate. From seven to nine titrations were made covering the increase from about 3 to 17% of enol.

The equilibrium values for rotation and enol content were obtained by adding more piperidine and allowing the mixture to stand at constant temperature. A series of concordant readings twelve hours apart were accepted as the equilibrium rotation and four of five titrations checking to about 1 part in 100 gave the average per cent. of enol.

Summary

1. Simultaneous measurements have been made of the rate of racemization and of enoli-

(13) Hickman and Sanford, *Rev. Sci. Instruments*, **1**, 152, Fig. 13 (1930).

(14) Hinrichsen and Kempf, *Ber.*, **46**, 2112 (1913).

(15) Vorländer and Wallis, *Ann.*, **345**, 285 (1906).

zation of menthyl α-phenylacetoacetate.

2. The results show that enolization takes place through some intermediate step. In this step nearly two-thirds of the racemization occurs, only one-third involving actual transformation to the enol.

3. Alternative explanations are offered, one involving loss of configuration in an intermediate anion, the other reversible formation of a small amount of open-chain enol followed by a slower accumulation of chelated enol.

DURHAM, N. H. RECEIVED JULY 7, 1936

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Determination of Activity Coefficients from the Potentials of Concentration Cells with Transference. II. Hydrochloric Acid at 25°

BY THEODORE SHEDLOVSKY AND DUNCAN A. MACINNES

In the first article of this series[1] it was shown that the activity coefficients, f, of chlorides in aqueous solution could be obtained from the potentials, E_t, of galvanic cells of the type

Ag; AgCl, MCl (C_1): MCl (C_2), AgCl; Ag (A)

with aid of the relation

$$E_t = \frac{2RT}{F}\int_{C_1}^{C_2} t \, \mathrm{d} \log Cf \qquad (1)$$

in which t is the transference number of the positive ion constituent, M, C is the concentration, and the other terms have their customary significance.[2]

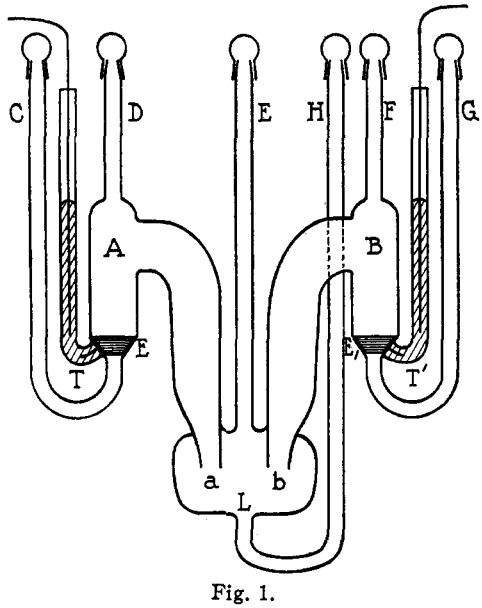


Fig. 1.

However, cells of type A contain a liquid junction and, until the present researches, have not been used to obtain activity coefficients. It was therefore decided to include hydrochloric acid in the series of measurements since the activity coefficients of that substance have been determined, with considerable accuracy, by various workers, using concentration cells without liquid junction of the form

Ag; AgCl, HCl (C_1); H_2 (Pt) — (Pt) H_2; HCl (C_2), AgCl; Ag (B)

Since cells of type B do not involve amalgam electrodes, with their attendant experimental difficulties, this case affords the most favorable comparison of the methods involving cells with and without liquid junction.

This paper will therefore deal with the determination of the potentials of the cell

Ag; AgCl, HCl (C_1): HCl (C_2), AgCl; Ag (C)

in which C_2 varied from about 0.003 to 0.08 N, and C_1 was 0.1 N. The results have afforded a test of the Debye-Hückel relations connecting the activity coefficients of aqueous solutions of hydrochloric acid with the concentration.

Apparatus and Experimental Procedure

Although the principle involved is the same as that utilized in the work of Brown and MacInnes[1] decided changes have been made in the apparatus used. The new cell is shown diagrammatically in Fig. 1. Instead of forming the silver–silver chloride electrodes on wire, as in the previous work, hollow truncated cones of platinum foil, indicated at E and E', are used. The outer surfaces of these cones are sealed into the glass, contact being made with the mercury in tubes T and T'. The chief advantage of electrodes of this design is that they are completely protected from mechanical disturbance of their active surfaces. This we have found to be essential if the reproducibility is to reach 0.01 mv. or better. The electrodes are plated with silver and chloridized electrolytically, using the precautions suggested by Brown.[3] It is also found desirable to wash the plated silver with

(1) Brown and MacInnes, THIS JOURNAL, **57**, 1356 (1935).

(2) For a derivation of equation (1) see MacInnes and Brown, *Chem. Rev.*, **18**, 335 (1936).

(3) Brown, THIS JOURNAL, **56**, 646 (1934).