the bromine compound is relatively insensitive to potassium, but gave no details of preparation or testing procedure. None of the other compounds tested at all approaches these two reagents in value.

Among the substituent radicals, the nitro group seems to be most important in rendering a compound effective, since without it solubilities of potassium salts increase tenfold and ratios decrease to less than one. This might have been predicted in view of the almost universal presence of the nitro or the nitrite group in potassium precipitants. Yet, curiously enough, 2,6-dinitrochlorobenzene-4-sulfonic acid gives a potassium salt more than twice as soluble as the salt of the mononitro derivative.[6] We have spent some time attempting to prepare the halogen-free compound, 3-nitrotoluene-5-sulfonic acid, for comparison with the other acids studied, but have not been able to obtain it free from isomers.

Summary

In an effort to improve 2-chloro-3-nitrotoluene-5-sulfonic acid as a precipitant for potassium, the sodium and the potassium salts of nine closely related acids have been synthesized and their solubilities at 30° determined.

Of these acids, only 2-bromo-3-nitrotoluene-5-sulfonic acid is equal in value to the chlorine compound.

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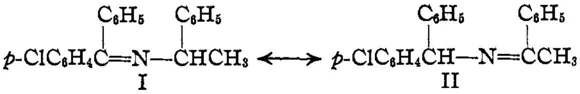
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Tautomerization of an Optically Active Azomethine

BY GERALD T. BORCHERDT AND HOMER ADKINS

Probably no one today seriously questions the concept of dynamic equilibrium in tautomerization, *i. e.*, that if A is in equilibrium with B, A is being converted to B and B is being converted to A. However, all the known *facts* bearing on this point *could* be rationalized on the assumption that the rate of conversion of A to B is progressively slowed up by the accumulation of B (and *vice versa*) so that at equilibrium A is not being converted to B, but is in a state which Michael called a "static" equilibrium.[1] It has seemed to us worth-while to ascertain by experiment whether in a given case, A is actually being converted to B at the rate predicted by the classical theory. This may be done by following the rate of a reversible rearrangement of an optically active substance by two methods, one of which depends upon the loss of optical activity and the other upon the concentration of the optically active compound plus the optically inactive compound resulting from the reversal of the reaction. If the rate of reaction calculated from the loss in optical activity is less than that found by the second method, support would be given to the concept of static equilibria. At the time these studies were begun (1930) no one, so far as we are aware, had ever determined the rate of a reversible reaction involving an optically active component, by two such methods. Since that time Ingold and his associates have made such measurements, having in mind objectives quite different from our own. However, their published data did not seem to us adequate for our purpose, since we were especially interested in the rate of reaction in the vicinity of equilibrium.

The rate of tautomerization of *l*-*p*-chlorobenzhydrylidene-α-phenylethylamine (I) to α-phenylethylidene-*p*-chlorobenzhydrylamine (II) has been measured by two independent methods. The tautomerization of I was made at 85° in alcohol using sodium ethoxide as a catalyst. The rate was determined (a) by noting the loss in rotatory power of the reaction mixture and (b) by determining with a polarograph the ratio of *p*-chlorobenzophenone to acetophenone resulting from the hydrolysis of the mixture of the two azomethines.



$$p\text{-ClC}_6H_4\overset{\overset{C_6H_5}{|}}{C}{=}N{-}\overset{\overset{C_6H_5}{|}}{C}HCH_3 \longleftrightarrow p\text{-ClC}_6H_4\overset{\overset{C_6H_5}{|}}{C}H{-}N{=}\overset{\overset{C_6H_5}{|}}{C}CH_3$$

I II

The rate of tautomerization of I was recently determined by Ingold and Wilson[2] who observed, first, the rotatory power of the α-phenylethylamine, and second, the chloride content of the mixture of hydrochlorides of α-phenylethylamine and *p*-chlorobenzhydrylamine, resulting from hydrolysis of the mixture of azomethines.

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(1) Michael and Leupold, *Ann.*, **379**, 263 (1911).

(2) Ingold and Wilson, *J. Chem. Soc.*, 1495 (1933); 92 (1934).

The rate of tautomerization in the present study was determined in six different series of experiments. In four of them the rate was followed by means of the polarograph upon optically inactive I, while in the fifth and sixth series the rate of reaction was determined upon optically active I by measuring the progressive loss in optical activity of the reaction mixture. Three polarographic determinations were also made in the sixth series.

TABLE I

DATA ON RATE OF TAUTOMERIZATION FROM POLAROGRAPHIC DETERMINATION OF RATIO OF ACETOPHENONE TO *p*-CHLOROBENZOPHENONE FROM HYDROLYSIS OF MIXTURES OF THE AZOMETHINES

Time, hours	Parts acetophenone in 100 parts of mixed ketones	$\text{Log}\ \frac{X - X_\infty}{X_0 - X_\infty}$	k
23	14.3	0.147	0.0147
41.3	19.4	.213	.0119
63.5	27.2	.342	.0124
94.1	34.3	.502	.0123
121	39.4	.672	.0128
143	42.1	.799	.0129
820	49.3	...	....
63.5	27.9	.354	.0128
88	34.2	.500	.0131
137.5	41.2	.740	.0124
161.5	43.5	.886	.0127
42.3	22.0	.252	.0137
66.4	28.5	.370	.0127
114.5	38.1	.628	.0127

The tautomerization is quite slow, the period of "half-life" at 85° being about 55 hours. The rate of reaction was followed for 160 hours with the polarograph and for 378 hours with the polarimeter. Polarographic determinations made after 820 hours showed that the ratio of I to II was 49.3 to 50.7. A plot of the log $(X - X_\infty)/(X_0 - x_\infty)$ against time indicated that at equilibrium the ratio was 50/50 as was also found by Ingold and Wilson.

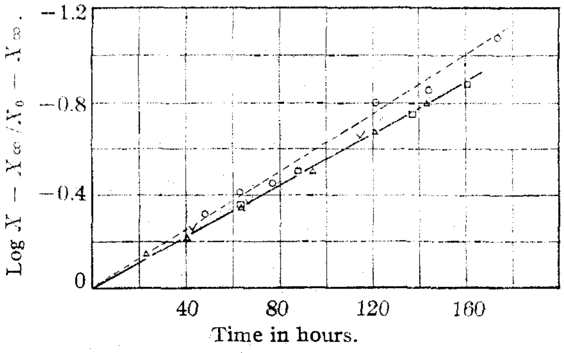

Fig. 1.—Polarographic determination of the rate of approach to equilibrium. The data from the first and third columns of Table I are plotted using △'s, ◻'s, and √'s to indicate the different series of experiments. The dotted line and the ○ represent the data of Ingold and Wilson.

The data upon the rate of tautomerization of I to II are given in Tables I and II. The data in Table I were obtained by determining the ratio of acetophenone to *p*-chlorobenzophenone in the hydrolyzate from the mixture of azomethines. The data in Table II are based upon a direct reading of the optical activity of the reaction mixtures in two series of experiments.

TABLE II

DATA ON RATE OF TAUTOMERIZATION FROM POLARIMETRIC DETERMINATION

Time, hours	Rotation (−)	% Conversion	$\text{Log}\ \frac{\alpha_0}{\alpha_t}$	k_1
0	1.370	...	....	......
12	1.265	7.7	0.035	0.00672
18	1.225	10.5	.049	.00627
36	1.065	22.2	.109	.00697
60	0.920	32.9	.174	.00668
86	.795	42.0	.236	.00632
136	.570	58.4	.378	.00641
161	.445	67.5	.488	.00699
180	.410	70.1	.522	.00668
278	.215	84.3	.806	.00668
0	1.295	...	....	......
19.8	1.165	10.0	.046	.00536
42.3	0.970	25.1	.125	.00678
66.4	.890	31.4	.163	.00566
114.5	.630	51.4	.313	.00630
162.8	.455	64.8	.454	.00643
210.0	.335	74.1	.587	.00644
258.0	.255	80.3	.706	.00630
308.0	.190	85.3	.834	.00625
378.0	.115	91.1	1.052	.00642

The data from Table I are plotted in Fig. 1. These show that for at least the first 160 hours the reaction proceeded smoothly, the value of the velocity constant being 0.0127 hours^{-1}. Ingold and Wilson calculated that the value of k was 0.0145 hours^{-1}, corresponding to the dotted line in Fig. 1.

The data from Table II are plotted in Fig. 2. In this case the solid line is not drawn through the experimentally determined points, but corresponds to the velocity constant calculated from the polarographic determinations of the ratio of ketones of Table I, where $k = k_1 + k_2$, and $k_1 = k_2 = 0.00635$ hours^{-1}. The polarographic determinations were not made beyond 160 hours, while the polarimetric determinations were made as high as 378 hours, when 91% of the optically active compound had tautomerized. Nevertheless, the experimentally determined values from the polarimeter fall very close to the line and there is an almost perfect agreement between the rates of the forward reaction as determined by the two methods. There is no evidence whatever that the rate of loss of optical activity was greater or less than the rate of tautomerization. There is no evidence for any side reaction occurring during nineteen days. The data are in perfect harmony with the concept of a dynamic equilibrium.

Incidentally the results are evidence of the usefulness of the polarograph as an instrument for determining the ratio of two ketones. The polarograph has also been useful, as shown in the experimental section, in indicating the purity of a given sample of an azomethine, since upon hydrolysis it showed the presence of a single ketone. Another sample of an azomethine was shown to be impure since the polarograms on its hydrolysis products showed two ketones.

Experimental Part

p-Chlorobenzhydrylidene-α-phenylethylamine (1) was prepared by essentially the same method as used by Ingold and Wilson. The oxime of acetophenone was obtained in 87% yield, m. p. 58–59°, from the reaction of 30 g. of acetophenone in 91 ml. of alcohol with 27.5 g. of hydroxylamine hydrochloride in 18.5 ml. of water, to which was added 50 g. of powdered sodium hydroxide. The oxime (50 g.) in 80 ml. of dry ethanol was hydrogenated within half an hour over Raney nickel (5 g.) at 125 atm. pressure. The α-phenylethylamine (neut. equiv. 121, b. p. 70° at 10 mm., n^{25}_{D} 1.5292) was obtained in 73% yield. If larger quantities of oximes were hydrogenated it was difficult to keep the temperature below 80°, with resultant low yields of amine.

p-Chlorobenzophenone was prepared as by Gomberg and Cone.[3] The ketone (417 g.) was obtained in 97% yield, starting with 2 moles each of chlorobenzene, aluminum chloride and benzoyl chloride. The product after three recrystallizations from alcohol–ether–water had a m. p. of 75.5–76°, as compared with 72–73° reported by Ingold and Wilson. Merz[4] obtained the same value as here reported. The dichloride of the ketone was made as previously described.[2] It was refractionated at 139° (0.2 mm.). The compound, analyzed for chlorine by the Thompson and Oakdale method, gave a value 0.07% high.

The azomethine I was prepared from 15 g. of the dichloride and 23.5 g. of the amine by heating them up very gradually to 100° and maintaining them there for four hours. The azomethine and amine were extracted with ether, and the amine precipitated with carbon dioxide. The extract was washed with water, 2% acetic acid and sodium bicarbonate solution, and finally dried over sodium sulfate. The azomethine was distilled from a bath at 200° under a pressure of less than 0.05 mm. The analysis for chlorine gave a value 0.09% high. The sample of azomethine I contained none of the tautomer II. This was shown by hydrolyzing some of the material and running a polarogram upon the ketone. The polarogram showed *p*-chlorobenzophenone free of acetophenone.

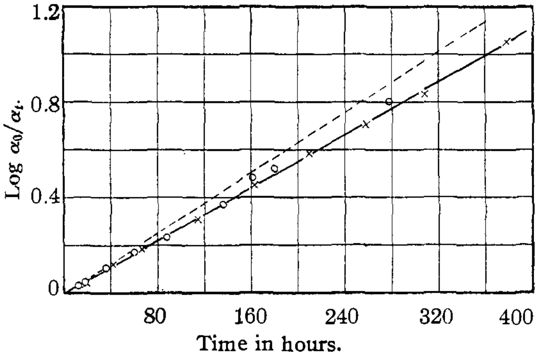

Fig. 2.—Polarimetric determination of the rate of approach to equilibrium. The data from the first and fourth columns of Table II are plotted using × and ○ to indicate the two series of experiments. The solid line represents the value of k_1 (0.00635 hrs.$^{-1}$) calculated from the polarographic determinations of Fig. 1. The dotted line represents the value of k_1 (0.0725 hrs.$^{-1}$) as calculated from the data of Ingold and Wilson.

d-α-Phenylethylamine (11.6 g.) was obtained from the *dl*-amine (50 g.) by the use of *l*-malic acid as by Ingersoll.[5] The rotation taken without a solvent in a 1-dm. semi-micro tube for $[\alpha]^{25}_{5873}$ was 39.24°.

The optically active azomethine was prepared by the same procedure used for preparing the *dl* mixture. About 5 g. of active azomethine was obtained from 9.8 g. of the active amine. The compound was analyzed for chlorine and nitrogen and gave values from 0.1 to 0.2% high. The values for the rotation of the azomethine determined in alcohol were as follows: $[\alpha]^{26}_{5873}$ −19.5°; $[\alpha]^{26}_{5461}$ −26.3°; (l = 1 dm., C = 7.73). After redistillation of the compound at 0.02–0.03 mm. the rotation was 0.8° lower than before.

We attempted to prepare the azomethine II from acetophenone and *p*-chlorobenzohydrylamine as by Ingold and Wilson. The product gave a high analysis for chlorine (1%) and upon hydrolysis gave polarograms indicating both acetophenone and *p*-chlorobenzophenone. These facts indicated that the azomethine had tautomerized to some extent and also contained *p*-chlorobenzhydrylamine. We failed to obtain acetophenone dichloride as by Ladenberg[6] so we could not use this compound for a synthesis similar to that used for I.

The procedure for the rate studies was improved in successive series of experiments, so the description given below applies in detail only to the fourth and sixth runs. Glass bulbs with a capacity of about 3 ml. were made so they could be evacuated through their capillary stems. In blowing the bulbs the breath was passed through a

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(3) Gomberg and Cone, *Ber.*, **39**, 3278 (1906).

(4) Merz, *ibid.*, **6**, 547 (1873).

(5) Ingersoll, "Organic Syntheses," Vol. XVII, John Wiley and Sons, Inc., New York, 1937, p. 80.

(6) Ladenberg, *Ann.*, **217**, 105 (1883).

drying tube. The bulbs were then heated while replacing the air in them with oxygen-free nitrogen. The bulbs were evacuated and the stems sealed off. These precautions are advisable in order to avoid contaminating the reaction mixture with water and oxygen, both of which have a deleterious effect. The stems were then broken off under the surface of the reaction mixture, which was made up from 36.8 ml. of dry ethanol, 1.05 g. of sodium and 1 g. of the azomethine I. The stems were again sealed off and immediately placed in the thermostat maintained at 85°.

After suitable intervals of from 20 to 820 hours the bulbs were removed from the thermostat and broken under 50 ml. of water. The samples were then extracted for four hours with 25 ml. of ether in a continuous extractor, the collection flask being heated at 80° in a water-bath. The ether was evaporated and the mixture of azomethines hydrolyzed with 2 ml. of 20% hydrochloric acid. The hydrolyzate was washed into the extraction apparatus with 10 ml. of ether and water added to a volume of about 50 ml. The solution was extracted with 10 ml. of ether for two hours, and then with 5 ml. of ether for one hour. The combined extracts were then made up to 100 ml. with alcohol.

The "standards" for the polarographic determinations were put through the same procedure. That is, weighed amounts of acetophenone and *p*-chlorobenzophenone were subjected to the procedure for hydrolysis and extraction. The procedure for the polarographic determination and the correction of wave heights has been given in an earlier paper.[7]

In making up the reaction mixture to be read in a polarimeter, it was found desirable to allow the sodium (after being weighed in xylene and washed in ether) to react for a few seconds with alcohol before being introduced into the absolute alcohol. This procedure gave a clear solution, free from colloidal matter, suitable for observation in a polarimeter.

The stems of the reaction bulbs after removal from the thermostat were broken off and the solution pipetted into a 2-dm. semi-micro polarimeter tube holding approximately 1.8 ml. The rotations were taken with the sodium D line in a Schmidt and Haensch number 52 B polarimeter.

The kinetics of the reaction are of the standard type for a unimolecular reversible reaction approaching equilibrium.[8] For the optically inactive system

$$\mathrm{X} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{Y} \qquad (1)$$

(where X is azomethine I and Y is II) the rate of formation of Y is then expressed by

$$\mathrm{d}y = k_1 x \,\mathrm{d}t - k_2 y \,\mathrm{d}t \qquad (2)$$

from which, by the proper substitutions of known equalities, there is obtained

$$\log \frac{\mathrm{X} - \mathrm{X}_\infty}{\mathrm{X}_0 - \mathrm{X}_\infty} = -\frac{k}{2.303}\, t \qquad (3)$$

where $k = k_1 + k_2$ as designated in (1). Hence plotting $\log (\mathrm{X} - \mathrm{X}_\infty)/(\mathrm{X}_0 - \mathrm{X}_\infty)$ against time (t) should give a straight line, the slope of which is equal to $k/2.303$.

For the optically active system

$$\mathrm{X}^* \xrightarrow{k_1} \overline{\mathrm{Y}} \underset{k_1}{\overset{k_2}{\rightleftharpoons}} \overline{\mathrm{X}} \qquad (4)$$

where X* designates the optically active isomeride I, $\overline{\mathrm{Y}}$ the *dl*-azomethine II, and $\overline{\mathrm{X}}$ the *dl*-azomethine I, formed from $\overline{\mathrm{Y}}$. The constants k_1 and k_2 are those described by (1).

$$\text{Hence } -\mathrm{d}x^*/\mathrm{d}t = k_1 t \qquad (5)$$

or

$$\log \alpha_0/\alpha_t = \frac{k_1}{2.303}\, t \qquad (6)$$

Summary

The rate of tautomerization of an optically active azomethine (1) has been determined by two methods. In the first the ratio of ketones produced by the hydrolysis of mixtures of the isomeric azomethines (I and II) has been determined by the use of a polarograph. In the second method the decrease in the optical activity of the mixture of azomethines has been observed as equilibrium was approached. The two methods agree perfectly, giving for k_1 a reaction velocity constant of 0.00635 hour^{-1}. The agreement between the two methods is evidence that the two azomethines are in dynamic equilibrium with each other.

The study has given evidence of the usefulness of the polarograph as a tool in the qualitative and quantitative analysis of mixtures of ketones.

MADISON, WIS. RECEIVED SEPTEMBER 7, 1937

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(7) Borcherdt, Meloche and Adkins, THIS JOURNAL, **59**, 2171 (1937).

(8) Hitchcock and Robinson, "Differential Equations in Applied Chemistry," John Wiley and Sons, Inc., New York, 1923, pp. 42-45.