3. It is shown that agreement between experimental activity coefficients and the predictions of the Debye–Pauling theory can be obtained by assuming that the ions in aqueous solution are hydrated and that they take part in an association equilibrium. The existence of such an equilibrium is shown to be in harmony with modern views of the structure of liquids.

4. Rough calculation yields values of the proper order of magnitude for the dissociation constants of the alkali halides. The relative values obtained for the different salts in this group are found to show some of the characteristic features observed in comparing their experimental activity coefficients.

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Polymolecular Solvolysis: Catalysis of the Racemization and the Hydrolysis of Optically Active α-Phenylethyl Halides by Polyhalide Metallic Salts

BY NICHOLAS T. FARINACCI

In previous studies,[1] the first order reactions of solvolysis were investigated to determine the type of mechanism involved in the alcoholysis of benzhydryl chloride and in the acetolysis of α-phenylethyl chloride. The optically active forms of the latter undergo reactions in hydroxylic solvents, such as water, the alcohols, acetic acid, etc., that yield products which are considerably racemized. A list of studies is included in Table I, for which both first and second order kinetics were observed.

TABLE I

HYDROLYSIS, ALCOHOLYSIS, ACETOLYSIS AND RACEMIZATION OF OPTICALLY ACTIVE α-PHENYLETHYL HALIDES IN VARIOUS SOLVENT MIXTURES

Ref.	Halide	Reaction medium	Temp., °C.
2	*d*-α-PhCHClMe	80% EtOH-H_2O	28.7
3	*d*-α-PhCHClMe	100% EtOH-$HgCl_2$	25
4	*l*-α-PhCHClMe	H_2O (two phases)	20
4	*l*-α-PhCHClMe	H_2O-KOH	20
4	*l*-α-PhCHClMe	60% Me_2CO-H_2O	70
4	*l*-α-PhCHClMe	80% Me_2CO-H_2O	70
4	*d*-α-PhCHClMe	100% MeOH	70
4	*d*-α-PhCHClMe	3.5 m. NaOMe in MeOH	70
4	*l*-α-PhCHClMe	100% EtOH	70
4	*l*-α-PhCHClMe	2.85 m. NaOEt in EtOH	70
4	*l*-α-PhCHClMe	H_2O	20
1b	*d*-α-PhCHClMe	100% HOAc	50
1b	*d*-α-PhCHClMe	100% Me_2CO, $N(Et)_4$-OAc	50
5	*l*-α-PhCHClMe	90 and 95% Me_2CO with	
5	*l*-α-PhCHClMe	$HgCl_2$ at various concns.	50
5	*l*-α-PhCHClMe	100% Me_2CO with $HgCl_2$	20
6	*l*-α-PhCHClMe	SO_2 with $N(Et)_4Cl$	..
7	*l*-α-PhCHBrMe	100% Me_2CO and Br^-	..

The generalization[8] that a second order displacement on an asymmetric carbon atom, the rate of which is proportional to the concentration of attacking ion, inverts the configuration is based on numerous studies. The validity of this principle was confirmed by experiments in which radioactive isotopes were used to follow the course of the substitution. When tagged iodide ions reacted with optically active halides, such as alkyl iodides, the specific rates were practically identical with the specific rates of racemization. This is required if every substitution on the asymmetric carbon atom inverts the configuration. Thus, the second-order reaction substantiated the stereo-

$$RI + I^{-*} \rightleftharpoons RI^{*} + I^{-}$$

chemical corollary of the London-Polanyi-Olson theory of substitution reactions that inversion was a part of the process. The R denotes the alkyl residue and the star refers to the radioactive isotope.[9]

The fact that a similar generalization could not be applied to the first-order substitution reactions of optically active halides offered a very interesting problem. One of the most logical explanations was that solvolytic reactions of this type involve carbonium ions which have a planar configuration and therefore result in racemized products.

The present study starts with the assumption that every substitution on an asymmetric carbon

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(1) (a) Farinacci and Hammett, THIS JOURNAL, **59**, 2542 (1937); (b) Steigman and Hammett, *ibid.*, **59**, 2536 (1937).

(2) Ward, *J. Chem. Soc.*, 445 (1927).

(3) Bodendorf and Boehme, *Ann.*, **516**, 1 (1935).

(4) Hughes, Ingold and Scott, *J. Chem. Soc.*, 1201 (1937).

(5) Read and Taylor, *ibid.*, 679 (1940).

(6) Bergmann and Polanyi, *Naturwissenschaften*, **21**, 378 (1933).

(7) Polanyi, Bergmann and Szabo, *Trans. Faraday Soc.*, **32**, 843 (1936).

(8) Meer and Polanyi, *Z. physik. Chem.*, **B19**, 164 (1932); Olson, *J. Chem. Phys.*, **1**, 418 (1933).

(9) Hughes, Juliusburger, Masterman, Topley and Weiss, *J. Chem. Soc.*, 1525 (1935); Hughes, Juliusburger, Scott, Topley and Weiss, *ibid.*, 1173 (1936); Cowdrey, Hughes, Nevell and Wilson, *ibid.*, 209 (1938).

atom inverts the configuration whether we are dealing with the bonds broken and formed in a solvolytic reaction or in a second-order displacement. In order to test the assumption, several processes that lead to the observed more or less extensive racemizations are analyzed to determine the part played by concurrent reactions. By the use of the following method, it can be concluded that the relatively high optical purity of the products obtained in the second-order substitutions depends on the fact that the substitution reaction is effectively isolated. On the other hand, because of the greater susceptibility to catalyzed racemization of the compounds which undergo solvolytic reactions, the substitution process is rarely isolated.

The analysis can be applied only to those studies where the time-variation of the optical rotation of the solution was recorded and also the data required for the calculation of the kinetics of the substitution process. In addition, it is necessary to include in the rate equations a characteristic constant, which is the ratio of the rotatory power of optically pure product and of optically pure starting compound. The complete data are available in very few reported studies.

The general theory is applied below to the experiments on the methoxylation of methyl α-bromopropionate.[10] The same systems were analyzed in terms of the partial rotations of the bromo and methoxy esters by Cowdrey, Hughes and Ingold. The present method verifies their conclusions and can be used to derive their equations. However, a few additional conclusions were derived in this presentation. The method was also applied to the solvolysis of optically active α-phenylethyl chloride in ethyl alcohol[3] in the presence of mercuric chloride. The success of the method suggests that it may clear up some obscure points in the phenomena of solvolytic reactions.

Solvolytic Methoxylation of Methyl α-Bromopropionate.—The reaction was run in pure methyl alcohol at 100° and calculated as a first-order substitution. As was pointed out by Ingold, *et al.*, four reactions which affect the rotation of the solution can be regarded as going on concurrently. They are a first-order hydrogen racemization on the alpha carbon atom, a second-order bromine racemization by the bromide liberated in the reaction, a corresponding hydrogen racemization of the methoxy ester after formation and the first-order methoxylation.

$$d\text{-RBr} \underset{k_2}{\overset{k_1}{\rightleftarrows}} l\text{-RBr} \qquad (1)$$

$$d\text{-RBr} + \text{Br}^- \underset{k_4}{\overset{k_3}{\rightleftarrows}} l\text{-RBr} + \text{Br}^- \qquad (2)$$

$$d\text{-RBr} + \text{MeOH} \xrightarrow{k_5} l\text{-ROMe} + \text{H}^+ + \text{Br}^- \qquad (3)$$

$$l\text{-RBr} + \text{MeOH} \xrightarrow{k_6} d\text{-ROMe} + \text{H}^+ + \text{Br}^- \qquad (4)$$

$$\text{R} = \text{CH}_3\underset{|}{\text{C}}\text{HCOOMe};\ k_1 = k_2;\ k_3 = k_4;\ k_5 = k_6$$

The complete equation for α, the optical rotation of the solution at time *t*, was derived as in the method given in detail for the mercuric chloride racemization of α-phenylethyl chloride in this paper. The solution is

$$\alpha_t = -\alpha_0 p/m \left\{ \frac{1}{bs} - \frac{(as-2)}{(bs)^2} \cdot\cdot + \cdot\cdot \frac{(as-2)(as-3)\ldots(as-n)\ldots}{(bs)^n} \right\} + \alpha_0 e^{(-bs+bsu)} u^{as} \left\{ u^{-1} - p/m \left(\frac{u^{-2}}{(bs)} - \frac{(as-2)}{(bs)^2} u^{-3} \ldots + \cdot\cdot \frac{(as-2)\,.\,.(as-n)u^{(-n-1)}}{(bs)^n} \right) \right\} \qquad (5)$$

The first expression on the right should reduce to the rotation at infinite time and is denoted α_∞. The ratio p/m is the quotient of the value of the rotation of optically pure product and of halide. Thus, it is a characteristic constant for this system. In equation (5), $b = k_3c_0$, $s = 2/k_5$ and $u = e^{-k_5t}$. The equations for the determination of k_1 and k_3 are derived below.

The change in the rotation due to the substitution alone will be

$$\alpha_s = \alpha_0((1 + p/m)e^{-k_5t} - p/m) \qquad (6)$$

That for the combined hydrogen racemization and the substitution is

$$\alpha_{s,h_r} = \alpha_0 \left(\frac{(2k_1 + k_5(1 + p/m))e^{-(2k_1+k_5)t} - p/mk_5}{(2k_1 + k_5)} \right) \qquad (7)$$

Their respective slopes are

$$\frac{d\alpha_s}{dt} = -\alpha_0 k_5(1 + p/m)e^{-k_5t}$$

and

$$\frac{d\alpha}{dt_{s,h_r}} = -\alpha_0(2k_1 + k_5(1 + p/m))e^{-(2k_1+k_5)t} \qquad (8a)$$

The value of k_1 depends on the difference of the slopes of the experimental curve and the substitution. After a very short time compared with

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[10] Cowdrey, Hughes and Ingold, *J. Chem. Soc.*, 1215 (1937).

the total reaction period, the relation (8b) will give the value k_1.

$$\frac{d\alpha_{exp}}{dt} - \frac{d\alpha_s}{dt} = -\alpha_0(2k_1 + k_5(1 + p/m)) + \alpha_0 k_5(1 + p/m) = -2k_1\alpha_0 \quad (8b)$$

This difference when divided by α_0 will give the value of the specific rate of the hydrogen racemization of the bromo ester.

Methoxylation of Methyl α-Bromopropionate with Methoxyl Ion.—This reaction was run in methyl alcohol at 25°. The hydrogen racemization was catalyzed by the methoxy ions, so that its rate is much greater than in pure alcohol. The bromide ion liberated in the reaction was not effective as a racemizing agent, but the methoxy-ion catalyzed and the hydrogen racemizations go on concurrently with the substitution.

$$l\text{-RBr} + \text{OMe}^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} d\text{-RBr} + \text{OMe}^- \quad (1)$$

$$l\text{-ROMe} + \text{OMe}^- \underset{k_4}{\overset{k_3}{\rightleftharpoons}} d\text{-ROMe} + \text{OMe}^- \quad (2)$$

$$l\text{-RBr} + \text{OMe}^- \xrightarrow{k_5} d\text{-ROMe} + \text{Br}^- \quad (3)$$

$$d\text{-RBr} + \text{OMe}^- \xrightarrow{k_6} l\text{-ROMe} + \text{Br}^- \quad (4)$$

$$\text{R} = \text{CH}_3\underset{|}{\text{C}}\text{HCOOMe};\ k_1 = k_2;\ k_3 = k_4;\ k_5 = k_6$$

The solution of the system of rate equations is obtained for this case by a transformation to a homogeneous linear equation with constant coefficients. Thus, the rotation of this reaction system at time t is

$$\alpha_t = \alpha_0\{(1 + c_0k_5t)^{-(2k_1 + k_5)/k_5} - \frac{p/m\alpha_0k_5}{(2k_1 - 2k_3 + k_5)}(1 + c_0k_5t)^{-(2k_3)/k_5} - (1 + c_0k_5t)^{-(2k_1 + k_6)/k_5}\} \quad (5)$$

The Solvolysis and Racemization of α-Phenylethyl Halides by $HgCl_2$, Ethyl Alcohol and $HgCl_3^-$.—In their study of the catalyzed racemizations of organic halides by metallic halides, Bodendorf and Boehme[3] compared the rate of change of optical rotatory power with the rate of alcoholysis of d-α-phenylethyl chloride in anhydrous ethyl alcohol in the presence of mercuric chloride. The data for the calculation of the rate constants was obtained by the titration of the acidity with 0.1 N potassium hydroxide. Satisfactory constants were obtained if the rates were assumed to vary as a higher power than unity of the concentration of metallic halide.

It is unlikely that chloride ion exists as such in this system, but more probably the complex ions, $HgCl_3^-$ and $HgCl_4^{--}$, are formed in the transition state by the combination of the separated Cl^- with $HgCl_2$ and $HgCl_3^-$. The $HgCl_3^-$ would then be expected to catalyze the racemization of organic chloride because of its tendency to accept a chloride ion to form $HgCl_4^{--}$. This conforms with the theory of "polymolecular solvolysis" which considers that molecular species such as hydroxylic solvents and metallic polyhalides of the type under study are active catalysts for influencing the extent of the distribution between the reactants and the transition state.[11]

With these assumptions, the foregoing method is applied to calculate the change in optical rotatory power that would be expected. The specific rates calculated by the equation

$$d(RCl)/dt = -k(RCl)(HgCl_2) \quad (1)$$

increase about 50% from zero time to 6.75 hours. An equation of the type

$$d(RCl)/dt = -k_5(RCl)(HgCl_2) - mk_5(RCl)(HgCl_3^-) \quad (2)$$

gives satisfactory constants over the whole range. Since the data were given in terms of the concentration of H^+, relations between the concentration of the latter and the $HgCl_3^-$, $HgCl_4^{--}$ formed in the course of the reaction must be derived. There is only one value of m in the integrated forms of equation (2) that will give a constant value of k_5 over the whole range.

If c_1 and c_0 are defined as the initial concentrations of $HgCl_2$ and d-α-phenylethyl chloride, respectively, x the moles of $HgCl_2$ converted to $HgCl_3^-$ in t hours, and y the moles of $HgCl_4^{--}$ formed during time t, then the concentrations will be for $HgCl_2$ equal to $(c_1 - x)$, $HgCl_3^-$ equal to $(x - y)$ and for RCl equal to $(c_0 - (x + y))$ equal to $(c_0 - H^+)$, since H^+ must equal at any moment $(x - y) + 2y$. Integration of the equations

$$\frac{d(c_1 - x)}{dt} = -k_5(c_0 - (x + y))(c_1 - x);$$
$$\frac{dy}{dt} = mk_5(c_0 - (x + y))(x - y) \quad (3)$$

yields

$$y = \frac{m(c_1 - x)}{(1 - m)} + c_1 - \frac{c_1^{(1-m)}(c_1 - x)^m}{(1 - m)},\ m \neq 1$$
$$y = c_1 - (c_1 - x) - (c_1 - x)\ln\frac{c_1}{(c_1 - x)},\ m = 1 \quad (4)$$

This system of equations requires that m equals 0.5 for the data given by Bodendorf and Boehme.[3]

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[11] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 167–183.

The corresponding value of k_5 is 0.27 mole per liter per hour.

The integrated equation for calculating k_5 is

$$k_5 = \frac{2}{t(c_0 - 2c_1)} \ln \frac{2c_1}{c_0} \frac{(c_0 - \mathrm{H}^+)}{(2c_1 - \mathrm{H}^+)} \qquad (5)$$

A special case of the general treatment exists when c_0 equals $2c_1$, which gives the equation

$$k_5 = \frac{\mathrm{H}^+}{tc_1(c_0 - \mathrm{H}^+)} \qquad (6)$$

For the general case, let $(c_0 - 2c_1)$ equal v, then the relations to be used in the equations for the optical rotation are

$$\mathrm{HgCl_2} = \frac{c_1 v^2}{(c_0\, e^{k_5vt/2} - 2c_1)^2}$$

$$\mathrm{HgCl_3^-} = \frac{2c_0c_1v(e^{k_5vt/2} - 1)}{(c_0\, e^{k_5vt/2} - 2c_1)^2}$$

$$\frac{\mathrm{d(HgCl_2)}}{\mathrm{d}t} = -\frac{k_5c_1c_0\, e^{k_5vt/2}\, v^3}{(c_0\, e^{k_5vt/2} - 2c_1)^3}$$

$$\frac{\mathrm{d(HgCl_3^-)}}{\mathrm{d}t} = \frac{(2c_0 - 2c_1 - c_0\, e^{k_5vt/2})k_5c_1c_0e^{\,k_5vt/2}v^2}{(c_0\, e^{k_5vt/2} - 2c_1)^3} \qquad (7)$$

The substitution reaction converts the optically active α-phenylethyl chlorides to the optically active phenylethyl ethyl ethers. For this system the ratio p/m is 1.465 calculated from the values, ethyl ether $\alpha^{20}{}_{\mathrm{D}}$ 74° and for optically pure chloride $\alpha^{20}{}_{\mathrm{D}}$ 50.6° (*cf.* ref. 4).

The reactions for the system are

$$d\text{-RCl} + n\mathrm{HgCl_2} \underset{k_2}{\overset{k_1}{\rightleftarrows}} l\text{-RCl} + n\mathrm{HgCl_2} \qquad (8)$$

$$d\text{-RCl} + \mathrm{HgCl_3^-} \underset{k_4}{\overset{k_3}{\rightleftarrows}} l\text{-RCl} + \mathrm{HgCl_3^-} \qquad (10)$$

$$d\text{-RCl} + \mathrm{HgCl_2} + \mathrm{HOEt} \xrightarrow{k_5} l\text{-ROEt} + \mathrm{HgCl_3^-} + \mathrm{H^+} \qquad (12)$$

$$\text{-RCl} + \mathrm{HgCl_2} + \mathrm{HOEt} \xrightarrow{k_6} d\text{-ROEt} + \mathrm{HgCl_3^-} + \mathrm{H^+} \qquad (13)$$

$$d\text{-RCl} + \mathrm{HgCl_3^-} + \mathrm{HOEt} \xrightarrow{k_7} l\text{-ROEt} + \mathrm{HgCl_4^{--}} + \mathrm{H^+} \qquad (14)$$

$$l\text{-RCl} + \mathrm{HgCl_3^-} + \mathrm{HOEt} \xrightarrow{k_8} d\text{-ROEt} + \mathrm{HgCl_4^{--}} + \mathrm{H^+} \qquad (15)$$

where n denotes the number of molecules of $\mathrm{HgCl_2}$ involved in the racemization. At high concentrations of $\mathrm{HgCl_2}$, a proportionality between the rate and a concentration of $\mathrm{HgCl_2}$ greater than unity has been observed.[3,5]

$$k_1 = k_2;\ k_3 = k_4;\ k_5 = k_6 = 2k_7 = 2k_8$$

The rate equations are

$$\mathrm{d}(d\text{-RCl})/\mathrm{d}t = -k_1(d\text{-RCl})(\mathrm{HgCl_2}) + k_2(l\text{-RCl})(\mathrm{HgCl_2}) - k_3(d\text{-RCl})(\mathrm{HgCl_3^-}) + k_4(l\text{-RCl})(\mathrm{HgCl_3^-}) - k_5(d\text{-RCl})(\mathrm{HgCl_2}) - k_7(d\text{-RCl})(\mathrm{HgCl_3^-}) \qquad (16)$$

$$\mathrm{d}(l\text{-RCl})/\mathrm{d}t = k_1(d\text{-RCl})(\mathrm{HgCl_2}) - k_2(l\text{-RCl})(\mathrm{HgCl_2}) + k_3(d\text{-RCl})(\mathrm{HgCl_3^-}) - k_4(l\text{-RCl})(\mathrm{HgCl_3^-}) - k_6(l\text{-RCl})(\mathrm{HgCl_2}) - k_8(l\text{-RCl})(\mathrm{HgCl_3^-}) \qquad (17)$$

$$\mathrm{d}(d\text{-ROEt})/\mathrm{d}t = k_6(l\text{-RCl})(\mathrm{HgCl_2}) + k_8(l\text{-RCl})(\mathrm{HgCl_3^-}) \qquad (18)$$

$$\mathrm{d}(l\text{-ROEt})/\mathrm{d}t = k_5(d\text{-RCl})(\mathrm{HgCl_2}) + k_7(d\text{-RCl})(\mathrm{HgCl_3^-}) \qquad (19)$$

The equation for alpha

$$\alpha = m(d\text{-RCl} - l\text{-RCl}) + p(d\text{-ROEt} - l\text{-ROEt}) \qquad (20)$$

gives the ratio of second and first derivatives

$$\frac{\mathrm{d}^2\alpha}{\mathrm{d}t_2} \Big/ \frac{\mathrm{d}\alpha}{\mathrm{d}t} = -(2k_1 + k_5)(\mathrm{HgCl_2}) - (2k_3 + k_7)(\mathrm{HgCl_3^-}) + \frac{(2k_1 + k_5(1 + p/m))\,\dfrac{\mathrm{d(HgCl_2)}}{\mathrm{d}t} + (2k_3 + k_7(1 + p/m))\,\dfrac{\mathrm{d(HgCl_3^-)}}{\mathrm{d}t}}{(2k_1 + k_5(1 + p/m))(\mathrm{HgCl_2}) + (2k_3 + k_7(1 + p/m))(\mathrm{HgCl_3^-})}$$

where the n of equation (8) has the value unity.

The use of equations (7) with the further substitutions, let $u = e^{k_5vt/2}$, $(2k_1 + k_5) = a$, $(2k_3 + k_7) = b$, $(2k_1 + k_5\,(1 + p/m)) = 1$, and $(2k_3 + k_7\,(1 + p/m)) = g$, $h = v(a - 2b)/k_5$, $r = (av - 2bc_0)/2c_1k_5$, yields

$$(e^{-R}\,\alpha - B)\,\frac{k_5v}{2} = \int e^{h/(c_0u - 2c_1)}\,\frac{(c_0u - 2c_1)^{r-2}}{u^{r+1}}\,(1v - 2gc_0 + 2gc_0u)\,\mathrm{d}u \qquad (22)$$

By the use of the transformation $s = u/(c_0u - 2c_1)$ and the substitution $w = (k_5\, r + 4k_3)/k_5$

$$-c_1ve^{w}(e^{-R}\alpha - B) = c_0w \int e^{c_0ws}s^{1-r}\,\mathrm{d}s + (p/m + 1 - r)\int e^{c_0ws}s^{-r}\,\mathrm{d}s$$

This sum of two integrals yields, when the exponential e^{c_0ws} is expanded and the integration constants R and B are evaluated

$$\alpha_t = \alpha_0 - \alpha_0e^{-wc_0/v} \left\{\left(1 + \frac{p/m}{1 - r}\right) + c_0w\left(1 + \frac{p/m}{2 - r}\right)\frac{1}{v} + \frac{c_0{}^2w^2}{2}\left(1 + \frac{p/m}{3 - r}\right)\frac{1}{v^2}\cdots\right\} + \alpha_0\, e^{-wc_0/v(sv)^{1-r}} \left\{\left(1 + \frac{p/m)}{1 - r}\right) + c_0w\left(1 + \frac{p/m}{2 - r}\right)^s + \ldots + \ldots\right\} \qquad (23)$$

which is an equation for the calculation of the value of the optical rotation in the system at any moment t (see Fig. 1).

The equation for the change in alpha due to the reactions (8, 12, 13, 14, 15) is derived in the same way and has correspondingly different values of the coefficients and powers of the exponential, but the same form. That for the substitution reactions, however, is simpler and has the form

$$\alpha_t = \alpha_0\,\frac{(vu + vup/m - c_0up/m + 2c_1p/m)}{(c_0u - 2c_1)} \qquad (24)$$

where v and u have the same values, *i. e.*, $v = (c_0 - 2c_1)$ and $u = e^{k_5vt/2}$.

The value of $2k_1$, the specific rate of the $HgCl_2$ catalyzed racemization, was derived as in the calculations made previously for the α-bromopropionic esters. It was found to have the value 0.135 mole per liter per hour if n in equation (8) is given the value unity. The value of $2k_3$, which brings the calculated and the experimental curves in close coincidence up to twenty hours, is 0.0337 mole per liter per hour.

Interpretation of the Data of Bodendorf and Boehme.—For the alcoholysis, the titer at 0 time was 1.5 cc. of 0.1 N potassium hydroxide which suggests that the organic halide contained preformed H^+, or the alternative suggestion that it was formed by reaction. The Tables II and III contain Bodendorf's and Boehme's data and corrections to conform with the first supposition above. On this basis, c_0 equals 0.36665 and c_1 equals 0.16952 mole per liter, initially.

TABLE II

TITRATION DATA OF BODENDORF AND BOEHME, TEMP. 25°

Min.	Hr.	N/10 KOH, cc.	Mole H^+ present	Mole H^+ formed
0	0	1.5	0.015	0.0
60	1	3.16	.0316	.0166
125	2.083	4.80	.048	.033
240	4.0	7.73	.0773	.0623
405	6.75	10.84	.1084	.0934
1360	23.666	20.74	.2074	.1924
3070	51.666	26.72	.2672	.2522
. .	. . . .	37.1	.371	.356

TABLE III

OPTICAL ROTATION DATA OF BODENDORF AND BOEHME, TEMP. 25°; c_0 = 0.3656, c_1 = *ca.* 0.169

Min.	Hr.	α
0	0	3.68°
150	2.5	2.65
310	5.166	1.65
410	6.833	1.17
1515	25.25	−0.87
3260	54.33	−1.35 (final value)

Discussion

The theoretical curve calculated by equation (23) diverges from the experimental curve after twenty hours. Several factors which were not taken into account might explain this divergence. Among these, the possible reversibility of the reaction, although not noted in the experiment, might still be appreciable. A definite reversibility in the acetolysis of α-phenylethyl chloride with pure acetic acid has been recorded.[1b] Side reactions such as the formation of styrene or the alcoholysis of mercuric chloride are known to occur in similar reactions.[5] Since the difference is small, it is not unlikely that it is due to such factors. The direct reaction of the halide with alcohol was relatively too slow to have more than a slight effect on the rotation when mercuric chloride also was present.

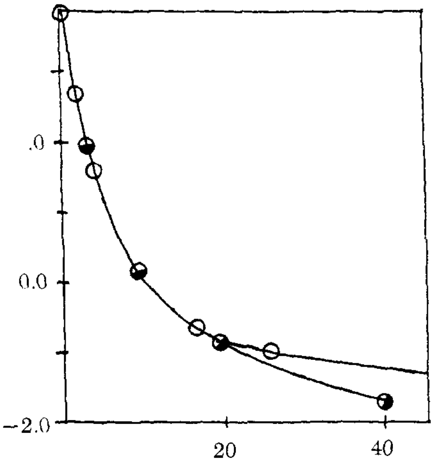

Fig. 1.—The optical rotation–time curve for the alcoholysis of *d*-α-PhCHClMe in EtOH with added $HgCl_2$ (data of Table III). ○ represents the experimental curve; ◑ the theoretical curve calculated by equation (23), example 3.

The three examples of the calculation of theoretical curves for the optical rotatory power of solutions where several reactions effect the change in the rotation have some novel features. In the method, there is introduced more complicated equations than are usually applied in rate calculations based on optical rotatory measurements. The characteristic constant, p/m, which has the value unity when a pure substance is transformed to its stereoisomer, must be independently determined as the ratio of pure substances.

The method should furnish precise equations for systems which are not too complicated where several reactions occur which depend either on the first or on higher powers of the concentration of the reagents. In addition to the given examples, the author has calculated the equations for the case where the $HgCl_2$ catalyzed racemization is proportional to the square of the $HgCl_2$, for the case where the substitution reactions do not invert the configuration and also the simpler equations that result when the concentration of the α-phenylethyl chloride is exactly double that of the mercuric chloride. Space does not permit the presentation of these.

The use of the method brings out the principal differences between second-order and first-order substitutions which are shown to depend on the relative isolation of the main reaction of substitution. The differences, of course, depend on the relative reactivity of the organic halides with specific reagents and are closely connected with structural and solvent effects. For reasons which have been given previously,[1] in reactions which involve hydroxylic solvents, such as water and the alcohols, we favor the "polymolecular interpretation" for the solvolysis of secondary and tertiary halides. When the solvent concentration is large and constant, the rate expression reduces to the first-order form. In the above examples, it is unnecessary to include the solvent concentration in the calculations.

If, for a given reaction which involves optically active molecules, ionization of the organic halide is definitely known to occur, this method should prove useful to calculate the degree of such ionization. The chief usefulness is for testing reaction mechanisms of the above type.

Summary

Rate equations were derived for the calculation of the change in the optical rotatory power of solutions in which several reactions proceed simultaneously. They were applied to three sets of experimental results for which the necessary data are sufficiently complete to test the equations. The agreement of theory and experiment is satisfactory in all cases and suggests the usefulness for the determination of reaction mechanisms.

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Studies on Cytochrome c. I. Electrophoretic Purification of Cytochrome c and its Amino Acid Composition*

BY HUGO THEORELL AND Å. ÅKESSON

It has been mentioned in a previous report[1] that cytochrome c, which was obtained in 1935 by H. Theorell[2] and in 1937 by Keilin and Hartree[3] with an iron content of 0.34%, could be further purified by electrophoresis to a hemin iron content of 0.43%. The preparation purified in this way, unlike the preparation with 0.34% iron, migrates uniformly on electrophoresis at different hydrogen ion concentrations. As the electrophoretic test for purity seems to be very delicate with such a low molecular substance as cytochrome (M = 13,000), which shows, moreover, an extremely unusual ion mobility curve,[4] there was good reason to suppose that cytochrome with 0.43% iron really represented a chemically homogeneous substance. Moreover, on account of the low molecular weight, it was possible by further analyses of the content of sulfur and various amino acids to obtain additional confirmation of the homogeneity of the cytochrome, since in a pure substance all the constituent parts occur in whole number proportions in the molecule. There was another reason why the amino acid analyses were of interest. Keilin and Hartree[3] reported that the content of basic amino acids in cytochrome with 0.34% iron differed little from that of hemoglobin. These values seemed to us to be incompatible not only with the ion mobility curve of cytochrome, which we had previously found to constitute an almost constant plateau between *p*H 6 and *p*H 9, indicating a very low histidine content, but also with the strongly basic character of cytochrome: its isoelectric point lies at *p*H 10, in contradistinction to that of hemoglobin (about *p*H 7). Our amino acid analyses showed that the pure cytochrome contains much less histidine (3.3%) and much more lysine (24.7%) than was shown by Keilin and Hartree's analyses (7.8 and 9.1% respectively). The low histidine content partly explains the flat course of the ion mobility and titration curves in the range within which the imidazole groups are titrated (*p*H 5.5–8.5, Wyman[5]). In connection with the titration curve it will be shown, moreover, that probably two of the three histi-

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* Reprints of this and the three following papers may be obtained from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California.

(1) H. Theorell and Å. Åkesson, *Science*, **90**, 67 (1939).

(2) H. Theorell, *Biochem. Z.*, **279**, 463 (1935).

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(4) H. Theorell, *Biochem. Z.*, **285**, 207 (1936).

(5) J. Wyman, *J. Biol. Chem.*, **127**, 1 (1939).