able from his own work and the data of previous papers to convert his specific activity to that in maleate buffer at *p*H 7 and 25°. He has given[3] the molecular weight of urease as 480,000 and evidence has been presented[15] that such a molecule contains four active sites. Thus the expression for k_3' per active site is found to be $k_3' = 7 \times 10^9 \exp(-8850/RT)$ sec.$^{-1}$. This is written as a unimolecular rate constant since the kinetic function of water is not known. The numerical magnitude of the pre-exponential factor is somewhat unusual, being much smaller than the median value for reactions involving small molecules.

From the data on the temperature dependence of the Michaelis constants in Table III the following expressions are readily obtained

$$\ln K_B = (-6.5 \pm 5)/R - (1600 \pm 1500)/RT \text{ and}$$
$$\ln K_B' = (-0.5 \pm 5)/R - (3100 \pm 1500)/RT$$

There has been considerable discussion in the literature concerning the kinetic meaning of the Michaelis constant. On the first glance the invariance of K' to changes in *p*H and solvent, as compared with substantial changes in V_m, suggests that $k_2' > k_3'$ and therefore that K' has the meaning of a thermodynamic equilibrium constant k_2'/k_1'. By the same argument, then, $K = k_3/k_1$. This is, of course, not impossible but another interpretation appears more likely. The values of V_m here reported are relative to the rates measured under a standard set of conditions. Hence $V_m = k_3'(E_0)/(k_3'(E_0))_{\text{standard}}$; it involves not only the dependence of k_3' but also that of (E_0) on such variables as *p*H, temperature, etc. It seems rather arbitrary to assume that the latter dependence is nil. Acid–base ionization equilibria[16] may result in a fraction of the catalytic sites being inactive. These equilibria may be the entire cause of the *p*H dependence of V_m, in which case the previous argument as to the nature of K' is invalid and the comments on the temperature dependence of V_m may have to be revised. It is clear that the interpretation of the nature of the Michaelis constant must await the elucidation of the complete mechanism of urea hydrolysis by urease.

CAMBRIDGE, MASS.

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(15) J. F. Ambrose, G. B. Kistiakowsky and A. G. Kridl, This Journal, **73**, 1232 (1951).

(16) L. Michaelis, *Biochem. Z.*, **33**, 182 (1911).

[Contribution from the Department of Chemistry, University of Colorado]

Mechanisms of Elimination Reactions. VII. The Alkaline Dehydrohalogenation of Chloro- and Bromo-Maleate and Fumarate[1]

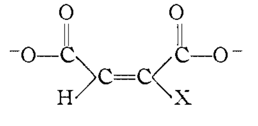
By Stanley J. Cristol and Arthur Begoon[2]

Received February 9, 1952

The kinetics of the alkaline dehydrohalogenation in water and in aqueous ethanol of the halofumarate ions and halomaleate ions have been studied. The determinations of the reaction order and of the effect of ionic strength upon rate constant have been interpreted to indicate that the reaction is between the bivalent ion of the salt and hydroxide ion. The extent of the superiority of *trans* over *cis* elimination has been measured, and this has been considered in terms of coulombic repulsions and in terms of mechanistic differences between *cis* and *trans* elimination.

In many bimolecular elimination reactions, a stereochemical preference is observed, *trans* substituents being more readily removed than corresponding *cis* substituents.[3] This paper is a continuation of a program relating to the factors contributing to relative reactivities in *cis–trans* systems. Two factors have been suggested as being of particular importance, one[4] involving *cis* repulsions and one[3,5] being based upon a postulated concerted one-stage mechanism for the *trans* process and a multiple-stage mechanism for the *cis* process.

As further tests of the relative importance of these factors, it seemed worthwhile to study the alkaline dehydrohalogenation of halomaleates (I) and halofumarates (II). Here, assuming that the attack is by hydroxide ion upon the hydrogen atom of the bivalent ion, it is seen that electrostatic repulsion will be greater between the negative hydroxide ion and the carboxylate group (which bears a whole negative charge) than between the hydroxide ion and the negative end of a carbon–halogen dipole. Thus if electrostatic repulsions were the determining factor in *trans vs. cis* elimination, the formation of sodium acetylenedicarboxylate from sodium halomaleate might be expected to be more rapid than from sodium halofumarate.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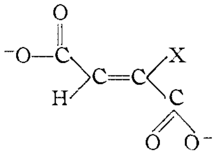
II

Michael[6] has reported that chlorofumaric and bromofumaric acids lose hydrogen halide more rapidly than the corresponding halomaleic acids upon treatment with excess aqueous alkali. In view of the fact that the argument given above is based upon reaction of the dicarboxylate ion, rather than upon either of the acid salts or the free acid with hydroxide ion, it seemed desirable to study the reaction more extensively than did Michael. Accordingly we have determined the

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[1] Previous paper in series: S. J. Cristol, N. L. Hause, A. J. Quant, H. W. Miller, K. R. Eilar and J. S. Meek, This Journal, **74**, 3333 (1952).

[2] Deceased December 15, 1951.

[3] Appropriate references have been given earlier (S. J. Cristol, N. L. Hause and J. S. Meek, This Journal, **73**, 674 (1951)).

[4] W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940).

[5] S. J. Cristol, This Journal, **69**, 338 (1947).

[6] A. Michael, *J. prakt. Chem.*, **52**, 289 (1895).

order of the reaction and have studied the effect of ionic strength upon the reaction rate, demonstrating that the reaction is indeed one between the bivalent anion and hydroxide ion; in addition we have measured the rates of reaction at various temperatures in water and in 54.2 wt. % aqueous ethanol and have calculated the quantities of activation for the four compounds from these data.

A consideration of the ionization constants for the 2-halo-2-butenedioic acids[7] shows that, in the basic media used in the rate experiments, the second ionization of the acid may be regarded as substantially complete. Thus, only if the reaction were between the dicarboxylate ion and hydroxide ion would the reaction be first order in organic halide and first order in hydroxide ion. Thus the determination of reaction order may be used to define the reacting species.

The usual test for second-order kinetics made by varying the concentration of each of the reactants separately and noting the constancy of the reaction-rate constant was inapplicable in this study, as it was found that the reaction involved the bivalent anion and hydroxide ion and was thus subject to primary salt effects. In any given run the ionic strength is invariant, acetylenedicarboxylate ion replacing halobutenedioate ion and halide ion replacing hydroxide ion. In accordance with this, each run was found to obey the second-order rate expression; as in many cases hydroxide was in large excess, obedience to this law proves the first-order relationship with respect to organic halide.

The variation of rate constant with ionic strength and the constancy of the rate constant when ionic strength was maintained constant and hydroxide ion or butenedioate concentration was varied are shown in Tables I and II. Sodium nitrate was used as neutral salt in these experiments. Thus, for bromomaleate ion, the variation of the second-order rate constant with ionic strength may be noted from Table I, experiments 1, 2, 3 and 5, and the fact that this was an ionic strength effect and not the effect of a reaction of higher order in hydroxide ion may be noted by a comparison of experiments 3 and 4, 5 and 6, and 7 and 8, where the substitution of nitrate ion for hydroxide ion did not affect the second-order rate constant. Analogous comparisons are available in Tables I and II for the other compounds. Thus the reactions were shown to be first order in hydroxide ion.

TABLE I

VARIATION OF THE SECOND-ORDER RATE CONSTANT WITH IONIC STRENGTH FOR THE DEHYDROHALOGENATION OF BROMOFUMARATE, BROMOMALEATE, CHLOROFUMARATE AND CHLOROMALEATE IONS IN 54.2 WT. % AQUEOUS ETHANOLIC SODIUM HYDROXIDE

Expt. no.	Ion	Temp., °C.	[Halide], *M*	[NaOH], *M*	$[NaNO_3]$, *M*	Ionic strength	10^4k, l./sec./mole
1	Bromo-maleate	61.40	0.00976	0.0717		0.112	4.73
2			.01455	.0621		.117	5.00
3			.00976	.1173		.163	6.40
4			.00983	.0716	0.0456	.163	6.59
5			.00996	.1626		.214	7.35
6			.00973	.0718	.0908	.213	7.41
7		39.77	.00974	.2522		.312	0.803
8			.00971	.1618	.0910	.313	0.810
9	Bromo-fumarate	45.12	.00974	.1167		.162	25.3
10			.00941	.0715	.0455	.162	27.6
11	Chloro-maleate	80.14	.00969	.0723		.112	2.48
12			.01460	.0625		.118	2.37
13			.00991	.1616		.212	3.91
14			.00977	.0722	.0909	.214	3.85
15	Chloro-fumarate	72.95	.00983	.1165		.162	17.7
16			.00977	.0708	.0456	.162	17.5
17			.00979	.1620		.212	21.8
18			.00977	.0712	.0908	.212	22.2

TABLE II

VARIATION OF THE SECOND-ORDER RATE CONSTANT WITH IONIC STRENGTH FOR THE DEHYDROHALOGENATION OF THE HALOFUMARATE AND HALOMALEATE IONS IN AQUEOUS SODIUM HYDROXIDE

Ion	Temp., °C.	[Halide], *M*	[NaOH], *M*	$[NaNO_3]$, *M*	Ionic strength	10^4k, l./sec./mole
Bromo-maleate	45.12	0.00969	0.0262		0.055	0.663
		.00967	.0262		.055	.627
		.00967	.0262	0.0252	.080	.746
		.00961	.0264	.0251	.080	.709
		.00965	.0263	.0502	.105	.810
		.00965	.0263	.0500	.105	.822
		.00972	.0718		.101	.781
		.00970	.0718	.0456	.147	.962
		.00963	.0719	.0455	.146	.902
		.00962	.0719	.0910	.192	1.03
		.00964	.0719	.0908	.192	1.03
		.00962	.0719	.1363	.237	1.09
Bromo-fumarate	45.12	0.00965	0.0263		0.055	12.5
		.00967	.0263	0.0250	.080	14.8
		.00971	.0262	.0502	.105	17.1
		.00962	.0719		.101	16.9
		.00961	.0719	.0455	.146	19.2
		.00974	.0717	.0908	.192	21.6
		.00970	.0718	.1363	.237	24.1
Chloro-fumarate	71.02	0.00987	0.0714		0.101	9.08
		.00996	.0712	0.0453	.146	10.5
		.00980	.0716	.0909	.192	12.2
		.00978	.0716	.1363	.237	12.7
		.00999	.0712	.2000	.301	14.6
Chloro-maleate	71.02	0.00993	0.0713		0.101	0.900
		.00991	.0713	0.0454	.147	1.08
		.00988	.0714	.0454	.147	1.06
		.00987	.0714	.0909	.192	1.13
		.00975	.0716	.1366	.238	1.23

Further evidence that the ions involved in the rate-determining step are the bivalent anion and the univalent hydroxide ion may be obtained by applying the Brönsted equation,[8,9] which relates rate constant and ionic strength. In this method logarithms of the specific reaction-rate constants are plotted against corresponding values of a function of the ionic strength, and approximate values of the product of the charges on the reacting species are obtained from the slope of the lines obtained.

From data of Table II, values for the product of the charges of +1.9 ± 0.2 for bromofumarate and +1.7 ± 0.2 for bromomaleate were obtained, as compared with the theoretical value of +2.0. Similar treatments of the data for the chloro systems give values of +1.6 and +1.3 as values for the product for chlorofumarate and chloromaleate, respectively.

Measurement of Reaction Rates.—The rates were determined in carbon dioxide-free water and in 54.2 weight % aqueous ethanol. In the work at 20 to 40°, a water-bath

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(7) N. W. Ashton and J. R. Partington, *Trans. Faraday Soc.*, **30**, 598 (1934).

(8) E. S. Amis, "Kinetics of Chemical Change in Solution," The Macmillan Co., Inc., New York, N. Y., 1949, p. 72.

(9) G. J. Doyle and N. Davidson, THIS JOURNAL, **71**, 3491 (1949).

maintained at constant temperature to within ±0.02° was used, the solutions were made up at the reaction temperature, and the reactions conducted in volumetric flasks. In the experiments at 50 to 90°, an oil-bath maintained at constant temperature ±0.04° was employed, and the reactions were run in sealed soft-glass test-tubes. The solutions were prepared at room temperature, aliquots were placed in test-tubes which were then sealed and placed in the thermostated bath. In these runs, the rate constants were corrected for the expansion of solvent.[10] The extent of reaction was followed by titration for halide ion by the Volhard procedure. Details of the procedures employed for the measurements and for the calculations of rate constants were substantially as described previously.[11,12] The results obtained are given in Tables I, II, III and IV. The data in Table III were obtained at an ionic strength of 0.11 molal and those in Table IV at an ionic strength of 0.10 molal.[13]

TABLE III

DATA AND SECOND-ORDER REACTION-RATE CONSTANTS FOR THE DEHYDROHALOGENATION OF BROMOMALEATE, BROMOFUMARATE, CHLOROMALEATE AND CHLOROFUMARATE IONS IN 54.2 WT. % AQUEOUS ETHANOLIC SODIUM HYDROXIDE AT AN IONIC STRENGTH OF 0.11

Ion	Temp., °C.	[Halide], *M*	[NaOH], *M*	Rate constant 10^4k, l./sec./mole
Bromomaleate	39.77	0.00991	0.0708	0.407
	49.90	.00982	.0716	1.25
		.00968	.0720	1.27
		.00970	.0719	1.30
			Av.	1.27
	53.59	.00954	.0725	2.13
	61.40	.00976	.0717	4.73
		.00977	.0721	5.06
		.01455	.0621	5.00
		.01457	.0626	4.97
			Av.	4.94
	73.31	.00973	.0721	17.4
		.00983	.0719	17.2
			Av.	17.3
Bromofumarate	45.12	.00970	.0714	18.7
		.00981	.0712	18.0
		.00971	.0714	18.7
		.00970	.0714	19.0
			Av.	18.6
	34.84	.00968	.0714	6.49
		.00973	.0713	6.41
			Av.	6.45
	23.36	.00985	.0711	1.67
		.00974	.0713	1.65
			Av.	1.66
Chromomaleate	69.49	.00983	.0720	0.830
		.00980	.0721	0.813
			Av.	0.822
	72.49	.00985	.0717	1.11
		.00981	.0717	1.10
			Av.	1.11
	73.31	.01060	.0703	1.21
		.00956	.0724	1.14
		.01043	.0707	1.08
			Av.	1.14
	80.14	.00969	.0723	2.48
		.00971	.0723	2.47
			Av.	2.48
	88.32	.00977	.0718	5.82
		.00961	.0721	5.98
			Av.	5.90
Chlorofumarate	61.53	.00973	.0713	3.84
		.00985	.0711	3.90
			Av.	3.87
	72.95	.00970	.0713	14.0
		.00984	.0711	13.8
			Av.	13.9
	81.05	.00985	.0710	31.4
		.00974	.0713	31.3
			Av.	31.4

TABLE IV

DATA AND SECOND-ORDER REACTION RATE CONSTANTS FOR THE DEHYDROHALOGENATION OF BROMOMALEATE, BROMOFUMARATE, CHLOROMALEATE AND CHLOROFUMARATE IONS IN AQUEOUS SODIUM HYDROXIDE AT AN IONIC STRENGTH OF 0.10

Ion	Temp., °C.	[Halide], *M*	[NaOH], *M*	Rate constant, 10^4k, l./sec./mole
Bromomaleate	45.12	0.00972	0.0717	0.781
		.00977	.0716	.755
			Av.	.768
	59.48	.00970	.0718	3.90
		.00973	.0717	3.72
			Av.	3.81
	71.02	.00974	.0717	12.2
		.00967	.0718	12.8
			Av.	12.5
Bromofumarate	23.38	.00979	.0716	1.95
		.00978	.0716	2.00
			Av.	1.98
	34.03	.00968	.0718	5.86
		.00965	.0719	5.77
			Av.	5.82
	45.12	.00962	.0719	16.9
		.00981	.0715	16.8
			Av.	16.9
Chloromaleate	71.02	.00986	.0714	0.930
		.00993	.0713	.900
			Av.	.915
	80.49	.00977	.0716	2.47
		.00981	.0715	2.46
			Av.	2.47
	90.63	.00991	.0713	6.79
		.00991	.0713	6.97
			Av.	6.88
Chlorofumarate	59.48	.00985	.0714	2.97
		.00995	.0713	2.89
			Av.	2.93
	71.02	.00977	.0716	9.24
		.00983	.0715	8.85
		.00987	.0714	9.08
		.00994	.0713	9.24
			Av.	9.10
	80.49	.00984	.0715	20.4
		.00991	.0713	20.5
			Av.	20.5

Activation energies were obtained from plots of log *k* *vs.* $1/T$ and entropies of activation were determined from these values and values of *k* read off these curves at 70.00°.[3] These values are given in Table V. We estimate the experimental uncertainties in E_{act} at about 0.7 kcal./mole and in $\Delta S^\ddagger$ at about 3 entropy units.

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(10) N. S. Osborne, E. C. McKelvy and H. W. Bearce, *Bull. Bur. Standards*, **9**, 327 (1913).

(11) S. J. Cristol, THIS JOURNAL, **67**, 1494 (1945).

(12) S. J. Cristol and N. L. Hause, *ibid.*, **74**, 2193 (1952).

(13) The experiments were conducted at approximately identical molarities in each solvent, but the ionic strengths differ in the two solvents due to differences in densities of the solvents.

TABLE V

ACTIVATION ENERGIES AND ENTROPIES OF ACTIVATION FOR THE DEHYDROHALOGENATION OF THE HALOFUMARATE AND HALOMALEATE IONS WITH SODIUM HYDROXIDE AT 70°

Ion	$10^4 k_{70°}$ l./sec./mole	E_{act} kcal./mole	$\Delta S^{\ddagger}_{70°}$ cal./mole/deg.
A. Solvent: water; ionic strength, 0.10			
Chlorofumarate	8.15	21.4	−13
Chloromaleate	0.809	25.7	− 5
Bromofumarate	115	17.5	−19
Bromomaleate	11.3	23.5	− 6
B. Solvent: 54.2 wt. % aqueous ethanol; ionic strength 0.11			
Chlorofumarate	9.96	25.3	− 1
Chloromaleate	0.832	26.2	− 3
Bromofumarate	204	20.8	− 8
Bromomaleate	12.3	24.2	− 4

Discussion of Results.—As noted in Table V the second-order rate constants for the halofumarate systems (II) in both water and aqueous ethanol at 70° are ten to seventeen times greater than those for the corresponding halomaleate systems (I). These results are in agreement with the semi-quantitative results of Michael.[6] It is to be further noted that the activation energies for the fumarates are lower than for the halomaleates. Calculations of the effect of electrostatic repulsions[14] indicate higher repulsions (and thus higher activation energies) for the halofumarates than for the halomaleates. As these calculations lead to predictions opposite to experimental results, we interpret the experimental results as indicating that the effect of electrostatic repulsion upon the energy of activation for elimination reactions is not of major importance (at least in solvents of sufficiently high dielectric constant).

The rate constants in aqueous ethanol are greater than those in water, in opposition to predictions from simple electrostatic theory.[15] The higher rate constants are the result of opposed effects in the quantities of activation. The higher activation energies observed are in accord with the simple electrostatic theory, but the greater effects of changing solvent upon the entropies of activation are superimposed upon these to give the larger rate constants. The inconsistency of rate constant and activation energy in mixtures of ethanol and water has been commented upon previously.[16]

The superiority of the *trans* process has also been attributed[3] to a difference in mechanism between it and the *cis* process. It was assumed that the *trans* process involved a one-stage concerted mechanism in which the proton was removed by base, the multiple bond was formed and the halide ion lost; the energy of the transition state was thus a reflection of these ionic bond strengths.[17] On the other hand, it was assumed that the *cis* process was multiple stage; the first and presumably rate-determining step involved the removal of a proton and the formation of a carbanion; the energy of the transition state was thus a reflection only of the carbon–hydrogen ionic bond strength. The difference between the heat of reaction of the rate-determining step of the *trans* process and that of the *cis* process is thus equivalent to the process, carbanion to olefin (or acetylene) plus halide ion, *viz.*

$$^{\ominus}\text{RC}{=}\text{CRX} \longrightarrow \text{RC}{\equiv}\text{CR} + \text{X}^- \qquad (1)$$

The data of Remick[18] were used for values of the carbon–chlorine and carbon–bromine ionic bond strengths; no value was available for the ionic bond strength involved in the ionization of the third bond in a triple bond. This was estimated as 250 kcal./mole by using the method of Remick and values of 123 kcal./mole for the bond strength of a carbon–carbon triple bond,[19] 100 kcal./mole for that of a double bond[19] and the values for ionization energy and electron affinity used by Remick for saturated atoms. Using these values, it was estimated that reaction (1) would be exothermic by 10 kcal./mole and 19 kcal./mole for the chloro and bromo systems, respectively.

If, following Polanyi,[17] it is assumed that there is a relationship between reaction heat and activation energy in analogous reactions, the decrease in activation energy being one-fourth to one-half the increase in heat of reaction, a prediction results that chlorofumarate will react with an activation energy 2.5 to 5.0 kcal./mole less than chloromaleate and bromofumarate 5 to 10 kcal./mole lower than bromomaleate. These predictions are in excellent agreement with the observed differences (see Table V) in water, values of 4.3 and 6.0 kcal./mole being observed.[20] This represents the second case[3] in which this test has been applied and the results have been analogous. It thus appears that these results furnish additional evidence regarding the proposed mechanistic differences between *cis* and *trans* elimination.

Materials Used.—Chlorofumaric acid was prepared by the method of Perkin.[23] It melted at 190–191° (Perkin reported 191–192° and Michael[6] 190–191°). Bromofumaric acid was prepared by the method of Michael.[6] It melted at 183–184°, whereas Michael reported 185–186°. We were unable to reproduce this melting point, although recrystallization from many solvents was tried. Bromomaleic acid, prepared according to Michael,[6] melted at 128–130° (recrystallized from nitromethane). Michael reported a melting point of 136–138°, but we were unable to

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[14] These calculations were made substantially as described previously for another case[3] giving estimates of the differences in coulombic energies involved in the approach of an hydroxide ion to within the transition-state distance of the hydrogen atom being removed, as affected by the *cis*- or *trans*-halogen atom and the *cis*- or *trans*-carboxylate group on the beta carbon atom.

[15] E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 657 (1941).

[16] S. J. Cristol and W. Barasch, THIS JOURNAL, **74**, 1658 (1952).

[17] R. A. Ogg and M. Polanyi, *Trans. Faraday Soc.*, **31**, 1375 (1935); M. G. Evans and M. Polanyi, *ibid.*, **34**, 11 (1938); E. T. Butler and M. Polanyi, *ibid.*, **39**, 19 (1943); M. Polanyi, *Endeavour*, **8**, 3 (1949).

[18] A. E. Remick, "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, p. 219.

[19] L. Pauling, "Nature of the Chemical Bond," Second Edition Cornell University Press, Ithaca, N. Y., 1940, p. 131.

[20] The question of values for bond energies is dependent upon the correctness of the value for the heat of sublimation of graphite and the values used above may be in error for this reason.[21,22] This question does not seem to be settled and calculations using the revised values[17,21,22] are qualitatively in the same direction as those indicated above.

[21] K. S. Pitzer, THIS JOURNAL, **70**, 2140 (1948).

[22] H. A. Skinner, *Trans. Faraday Soc.*, **41**, 645 (1945).

[23] W. H. Perkin, *J. Chem. Soc.*, **53**, 695 (1888).

duplicate this. Ingold and Chandrasena[24] reported a melting point of 128° for this material. Chloromaleic acid was prepared by hydrolysis of the anhydride.[25] It melted at 109.5–110° (reported 114–115°).[25]

All of the compounds gave excellent correspondence to the second-order rate equation and the theoretical halogen production, with the exception of chloromaleic acid which gave 97% of the theoretical chloride ion and rate constants which drifted down slightly at beyond 60% completion. These were corrected for by using the 97% figure as theoretical and determining rate constants before 60% completion.

Acknowledgment.—The authors are grateful for the support of this work under a contract with the Office of Naval Research. We also wish to thank Mr. Stanley Gebura for his aid in the preparation of the halofumaric acids.

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[24] J. P. C. Chandrasena and C. K. Ingold, *J. Chem. Soc.*, **121**, 1306 (1922).

[25] A. Michael and G. Tissot, *J. prakt. Chem.*, **52**, 331 (1895).

[CONTRIBUTION FROM GIBBS LABORATORY, DEPARTMENT OF CHEMISTRY, HARVARD UNIVERSITY]

The Molecular Weight and Shape of Desoxypentose Nucleic Acid

BY PAUL DOTY AND BARBARA H. BUNCE[1]

RECEIVED MAY 8, 1952

The angular distribution of the reduced intensity of light scattered from solutions of three desoxypentose nucleic acid samples (Gulland and Jordan, Schwander and Signer, and our own) over the concentration range of 5 to 20 × 10^{-5} g./cc. in 0.2 *M* NaCl has been determined. From this it is deduced that the molecular weights are 4.0, 6.7 and 4.0 million, respectively, and the maximum dimension of the Schwander and Signer sample is 6400 Å. Molecular shapes that are consistent with the scattering envelope are discussed.

In contrast with the recent progress in the chemical investigation of the structure of desoxypentose nucleic acid, DNA, physical studies have not led to a consistent view of the molecular weight and shape of this critically important macromolecule. The obstacles to successful physical studies have been twofold. First, various methods of preparation undoubtedly produce samples having different physical properties. These differences appear to be due to varying degrees of degradation. However, the recent introduction of milder methods of extraction and protein removal together with an increasingly effective inactivation of degrading enzymes offers hope that samples approaching closely the native molecules of DNA can be prepared. Second, it appears that none of the older methods of molecular weight and shape determination are adequate for the present problem, at least in the form in which they have been employed. This conclusion deserves some elaboration.

Chemical studies show that DNA is principally a polynucleotide carrying both strong and weak electrolytic groups. The magnitude of the double refraction of flow and the sedimentation constant show that most preparations yield large, asymmetric molecules whose molecular weight must be of the order of magnitude of one million. Thus the problem lies in characterizing a polyelectrolyte of unknown macrostructure. Indeed this is a most demanding problem as the small number of successful studies of the molecular weight and shape of polymeric electrolytes of known chain structure testify. The methods that have been applied to the problem are the following: sedimentation velocity,[2-6] diffusion,[2b-4] streaming birefringence,[7-11] dielectric dispersion[12] and the Kerr effect.[13] There have been numerous investigations of the viscosity of DNA solutions but thus far no one has succeeded in extrapolating to zero gradient. Until this is done precise molecular information cannot be expected from this source. Of the methods applied, only the combination of sedimentation and diffusion using the Svedberg equation leads to a molecular weight determination. An examination of the diffusion data shows that it has not been possible to carry out the measurements at sufficiently low concentrations to permit an unambiguous interpretation. Indeed the Schlieren curves reveal such marked asymmetry and the concentration dependence of the diffusion constant differs so radically from one investigation to another that it appears that no reliable estimate of the molecular weight is possible by this method. The osmotic pressure method is clearly too insensitive for use here and apparently has not been tried. One concludes therefore that no satisfactory determination of the molecular weight of DNA has been carried out except possibly on very degraded samples which are not considered here. In contrast there is complete unanimity among the methods listed above concerning the marked asymmetry of the DNA molecule. The quantitative interpretation of the data is however severely limited because only ellipsoidal models have been employed in deriving the relation between size and experimental effect. Making the arbitrary assumption that the DNA molecule is rod-like, streaming birefringence measurements on what appears to be the least degraded sample[10,11] lead to lengths of about 8000 Å.

The recently established techniques of light

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