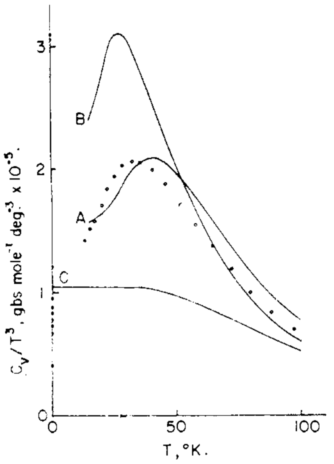

Fig. 1.—C_v/T^3 *vs.* T^3 for lithium chloride. The circles represent the experimental data. The curves are based on (A) the optical branch model with $\theta_D = 310$, $\theta_E = 250$ chosen empirically, (B) a calculation due to Karo (footnote 11) and (C) a Debye function with $\theta_D = 450$.

TABLE IV

Substance	T_M, °K.	$10^2\sqrt{ac_{11}/\mu}$ [11] cgs. units × (moles)$^{1/2}$	$T_M/\sqrt{ac_{11}/\mu}$
LiCl	33	4.94	6.7
NaI	12	2.28	5.3
KCl	17	2.86	5.9
KBr	12	2.30	5.2
KI	9.5	2.00	4.7

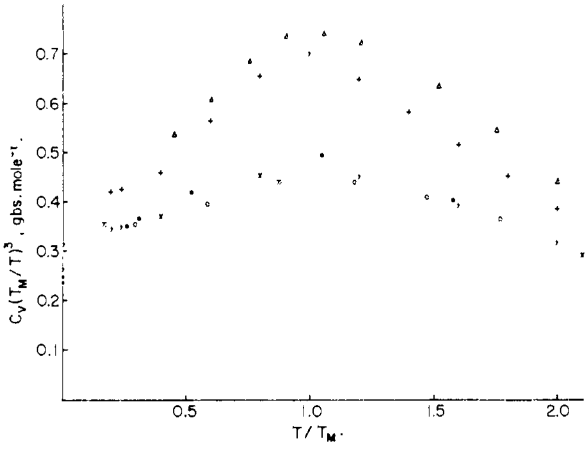

Fig. 2.—A reduced plot of $C_v(T_M/T)^3$ for several alkali halides(○ , KCl; ×, KBr; +, NaI; ●, KI; △, LiCl).

One further correlation which may be made consists of comparing T_M with the quantity $\sqrt{(ac_{11})/\mu}$. According to the model

$$T_M \; \alpha\omega\alpha \; \sqrt{ac_{11}/\mu} \tag{2}$$

The results are collected in Table IV. While the ratio is not constant within experimental error, there is a strong correlation, considering the range of the parameters.

Acknowledgments.—The author wishes to thank L. Murch and J. B. Ott for assisting with the experimental measurements, Virginia Shirley for help with the calculations and especially Professor W. F. Giauque for his continuing interest in this work.

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[11] The values of c_{11} were obtained from A. M. Karo, reported in University of California Radiation Laboratory Report UCRL 5525 (1959), and from ref. 9.

[CONTRIBUTION FROM THE PHYSICOCHEMICAL RESEARCH DIVISION, U. S. ARMY CHEMICAL WARFARE LABORATORIES, ARMY CHEMICAL CENTER, MARYLAND]

Properties, Interaction and Esterification of Methylphosphonic Dihalides

BY B. M. ZEFFERT, P. B. COULTER AND HARVEY TANNENBAUM

RECEIVED NOVEMBER 21, 1959

The mechanism of the formation of Sarin by the esterification of methylphosphonic dihalides with 2-propanol has been elucidated from physicochemical considerations, and evidence for the extent and rate of metathesis of an equimolar mixture of methylphosphonic dichloride and methylphosphonic difluoride is presented. The densities, viscosities, molar polarizations, dipole moments, refractive indexes, vapor pressures, freezing points and infrared spectral data of the dihalides were obtained, as well as the solid-liquid phase relations of the dichlor-difluor system.

The final step in the synthesis of isopropyl methylphosphonofluoridate (Sarin) involves the reaction of 2-propanol with an equimolar mixture of methylphosphonic dichloride and methylphosphonic difluoride (hereafter termed dichlor and difluor, respectively). The over-all reaction is

$$CH_3P(O)Cl_2 + CH_3P(O)F_2 + 2(CH_3)_2CHOH \longrightarrow 2CH_3P(O)(F)OCH(CH_3)_2 + 2HCl \tag{1}$$

Studies of the mechanism of this reaction were made in Germany after the initial preparation of Sarin by Schrader and also in England and in this country after World War II. Based on observations of the ease of reaction and of the nature and relative quantities of products formed in reactions of derivatives of methylphosphonic acid, Perry[1] postulated a sequence of reactions

$$CH_3P(O)Cl_2 + (CH_3)_2CHOH \longrightarrow CH_3P(O)(Cl)OCH(CH_3)_2 + HCl \tag{2}$$

$$CH_3P(O)F_2 + (CH_3)_2CHOH \xrightarrow{HCl} CH_3P(O)(F)OCH(CH_3)_2 + HF \tag{3}$$

$$CH_3P(O)(Cl)OCH(CH_3)_2 + HF \longrightarrow CH_3P(O)(F)OCH(CH_3)_2 + HCl \tag{4}$$

These are accompanied by the side reaction

$$CH_3P(O)(Cl)OCH(CH_3)_2 + (CH_3)_2CHOH \longrightarrow CH_3P(O)[OCH(CH_3)_2]_2 + HCl \tag{5}$$

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[1] B. J. Perry, Ministry of Supply, U.K., unpublished report.

A significant fact in support of Perry's postulations was his observation that production of small amounts of $CH_3P(O)[OCH(CH_3)_2]_2$ was accompanied by recovery of equivalent amounts of difluor.

This is essentially the same mechanism originally proposed by German workers, as reported by Collomp.[2] The possibility that methylphosphonic chlorofluoride (hereafter termed chlorfluor) participates as an intermediate in reaction 1 was considered, but evidence was limited due to the absence of information on the thermodynamic and kinetic behavior of the reaction

$$CH_3P(O)Cl_2 + CH_3P(O)F_2 \rightleftharpoons 2CH_3P(O)ClF \quad (6)$$

If reaction 6 proceeds sufficiently rapidly, a mechanism other than that proposed by Perry would be required for reaction 1.

The existence of equilibrium mixtures of a tervalent phosphorus compound and its disproportionation products has been reported.[3] There is also unpublished information on the disproportionation of Sarin. The chief objectives of the work described here were to investigate the behavior of reaction 6 and the mechanism of reaction 1.

Chemical analytical methods were not available for identifying the molecular species in dichlor–difluor solutions, and it was hoped that certain easily-measured physicochemical properties could be used in the investigation of reaction 6.

The techniques used included measurement of infrared absorption, molar polarization, molar freezing-point depression and solid-liquid phase relations, density, vapor pressure, viscosity and refractive index. The properties of the individual components and of the equimolar dichlor–difluor mixture were measured and compared to obtain evidence on the postulated equilibrium in reaction 6.

Materials. Several samples of methylphosphonic dichloride[4] were used. Purity, based on freezing point and heat of fusion,[5] ranged from 98.92 to 99.97 mole %. The methylphosphonic difluoride[6] was 99.72 mole % pure.[5] The methylphosphonic chlorofluoride[7] purity ranged from 95 to 99.7 mole %.[5]

Physical Properties.—Because of the moisture sensitivity of the methylphosphonic dihalides all sample transfers were made in a controlled-atmosphere box at relative humidities of 10% or lower. Thermostatically-controlled water baths regulated to ±0.03° were used for all except refractive index measurements.

Density.—Measurements were made with a glass dilatometer constructed from a 1-ml. precision pipet with 0.01-ml. divisions; a 10-ml. bulb was sealed to the pipet. The dilatometer was calibrated with freshly-boiled distilled water. Readings were made to ±0.002 ml. and calibration curves were prepared using published density values for water.[8] The precision of the density values was 0.0002 g./ml.

Freezing Point.—Determinations of freezing (or melting) points to ±0.05° or better were made by analysis of the time–temperature plots obtained during controlled cooling (or warming) of the samples in a thermistor-equipped cryostat.[9] The apparatus was modified by attaching an outer jacket to the sample compartment by means of a ring seal. Cooling rates were controlled by evacuation of the jacket through a side arm. Inoculation was effected with crystals of the same sample if excessive supercooling was experienced. Freezing points were followed by melting point determinations on the same sample in the cryostat.

Molar Polarization and Dipole Moments.—Dielectric constants were measured in benzene solution by the heterodyne beat method.[10,11] The benzene was specially purified by the method described by Smyth and Walls.[12] The dielectric cell was constructed according to Smyth and Morgan.[13] The materials of construction of the cell were changed because of the reactivity of the compounds; the cell consisted of three concentric platinum cylinders held apart by Teflon spacers. Molar polarization values were computed by the method of Halverstadt and Kumler,[14] from data obtained at two dilute concentrations. Neglecting the small atomic polarizations, the dipole portions of the total polarizations were obtained by subtracting the molar refractions, R_D, (obtained with the sodium D line) form P_∞ the molar polarizations at infinite dilution. Dipole moments were calculated from the Debye equation $\mu = 0.01281[(P_\infty - R_D)T]^{1/2}$. The error in the dipole moment measurement is considered to be less than 0.05 Debye unit.

Refractive Index.—Measurements of dichlor and difluor were made with an Abbe refractometer using sodium light and of chlorfluor with a Fisher refractometer (Fisher Scientific Co.). The prisms of the Abbe refractometer were regulated to ±0.05°; the Fisher instrument was used at room temperature.

Viscosity.—Measurements were made with Cannon viscometers that had been calibrated with fresh samples of viscosity oils certified by the National Bureau of Standards. Both arms of the viscometers were capped with $CaSO_4$-filled drying tubes to avoid moisture pickup during determinations. Flow times were small enough to require use of the kinetic energy correction term to Poiseuille's equation. No corrections were applied for expansion of the liquids from 25 to 50°. The precision of the viscosity measurements was ±0.01 centistoke.

Densities, freezing points, molar polarizations, dipole moments, refractive indexes and viscosities are given in Table I.

Vapor Pressure and Heat of Vaporization.—Vapor pressure values for dichlor and chlorfluor were obtained with an isoteniscope of the design described by Smith and Menzies.[15]

After the value at the highest temperature was obtained with each compound, check determinations were made at successively lower temperatures to observe any evidence of decomposition. Appreciable decomposition would have been indicated by vapor pressure values differing from those originally obtained. No changes were noted in the values measured. McGrath[16] has reported data obtained (by the method of Ramsay and Young[17]) with difluor of unstated purity. His data yield a value of 47 mm. at 30° compared to a single value of 44 mm. at 30° obtained in these Laboratories by the transference method[18] with a sample 99.72 mole % pure. The vapor pressure data for the three compounds were fitted to Antoine equations of the form $\log P = A - B/(t + k)$, where P is vapor pressure in mm., t is temperature in °C. and A, B and k are constants. The constants are shown in Table II.

Heats of vaporization were calculated from the vapor pressure data by the use of the Clausius–Clapeyron equation. The values were 10.6 kcal./mole (60 to 161°) for dichlor,

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[2] Collomp, Bull. Inf. Scient. Min. Guerre (Sect. techn. de l'Armee), 23/G (1949 Paris).

[3] F. W. Hoffmann, R. G. Roth and T. C. Simmons, THIS JOURNAL, **80**, 5937 (1958).

[4] A. M. Kinnear and E. A. Perren, *J. Chem. Soc.*, 3437 (1952).

[5] See footnotes of Table I and ref. 21 for freezing point and heat of fusion of purified material.

[6] T. P. Dawson and K. C. Kennard, *J. Org. Chem.*, **22**, 1671 (1957).

[7] F. W. Hoffmann, paper to be submitted for publication.

[8] L. W. Tilton and J. K. Taylor, *J. Research Natl. Bur. Standards*, **18**, 205 (1937).

[9] B. M. Zeffert and S. Hormats, *Anal. Chem.*, **21**, 1420 (1949).

[10] C. P. Smyth, "Dielectric Constant and Molecular Structure," Chemical Catalog Co., New York, N. Y., 1931, Chapter 3.

[11] Jen-Yuan Chien, *J. Chem. Educ.*, **24**, 494 (1947).

[12] C. P. Smyth and W. S. Walls, THIS JOURNAL, **54**, 1854 (1932).

[13] C. P. Smyth and S. O. Morgan, *ibid.*, **50**, 1547 (1928).

[14] I. F. Halverstadt and W. D. Kumler, *ibid.*, **64**, 2988 (1942).

[15] A. Smith and A. W. C. Menzies, THIS JOURNAL, **32**, 1412 (1910).

[16] L. B. McGrath, Ministry of Supply, U.K., unpublished report.

[17] W. Ramsay and S. Young, *J. Chem. Soc.*, **47**, 42 (1885).

[18] H. V. Regnault, *Ann. Chim.*, **15**, 129 (1845).

TABLE I

PHYSICAL PROPERTIES OF METHYLPHOSPHONIC DIHALIDES

		Dichlor	Difluor	Chlor-fluor	Equimolar dichlor-difluor mixture
Density, g./ml.	25.0°	1.4559^a	1.3595	1.4032	1.4078
	35.0°	1.4421	1.3410	1.3874	...
	50.0°	1.4213	1.3129	1.3636	...
Freezing Point, °C.		32.74^b	-36.92^c	-22.8^d	10.0
Molar Polarization (P_∞), cc. 25°		265.4	248.5	259.1	249.2
Dipole Moment		3.43	3.39	3.44	3.36
Refractive Index, n_D		1.4569^{35}	$1.3148^{25.0}$	1.350^e	1.408^e
Viscosity, centistokes	25.0°	1.39^a	0.57	0.82	0.92
	35.0°	1.16	.50	.71	.78
	50.0°	0.93	.42	.59	.65

[a] Supercooled liquid. [b] Furukawa, *et al.*,[15] found triple pt. 32.992° with 99.99 mole % sample. [c] Furukawa, *et al.*,[15] found triple pt. −36.81° with 99.89 mole % sample. [d] Furukawa, *et al.*,[19] found triple pt. −22.52° with 99.68 mole % sample. [e] Measured at room temp. with Fisher refractometer.

TABLE II

VAPOR PRESSURE CONSTANTS FOR METHYLPHOSPHONIC DIHALIDES

Compound	Purity, mole %	A	B	k	Range, °C.	Dev. from exptl., %
Dichlor	98.9	7.2442	1669.7	216.1	39–167	1
Difluor	Ref. 17	7.5444	1577.8	238.6	19–99	1
Chlorfluor	97.9	6.7123	1215.1	186.4	25–121	1

8.81 kcal./mole (19 to 99°) for difluor and 9.88 kcal./mole (25 to 121°) for chlorfluor.

Comparison of Properties.—In all the physical properties measured the equimolar dichlor–difluor solution exhibited close-to-ideal behavior. That this is also true for the freezing point will be shown below by the phase diagram. Except for the refractive index and the freezing point, values for the chlorfluor were so close to those obtained with the equimolar mixture that no good means of estimating the metathesis of the mixture was afforded. It was decided not to use refractive index measurements for our purpose because of the etching of the refractometer prisms produced by the fluorine-containing compounds. Solid-liquid phase equilibrium and later infrared spectroscopy were used to obtain more quantitative estimations of the presence of chlorfluor.

Phase Diagram.—The phase diagram of the dichlor-difluor system was constructed from freezing points at 13 separate compositions. All experimental points were obtained with freshly prepared solutions. Some were repeated with week-old solutions to check for slow reaction between the components. The results are shown in Table III. The results showed that the binary system consists of one liquid phase above 32.74°, the freezing point of the dichlor used, and that the liquid phase consists of essentially ideal solutions. There was one eutectic point, no solid addition compounds and no solid solutions. The molar freezing point depressions, C,[20] were calculated for each component. C was constant at 3.44 ± 0.02 for dichlor containing up to 25 mole % difluor solute. From pure difluor to the eutectic the solubility line deviated from ideality by an amount detectable by the sensitivity of the measurements, but probably attributable to impurity in the difluor. C for difluor, obtained by extrapolation to infinite dilution, was 2.34. The calculated heats of fusion were 4.81 and 2.53 kcal./mole for dichlor and difluor, respectively.[21]

TABLE III

DICHLOR–DIFLUOR SYSTEM

Composition, mole % dichlor	Freezing point, °C.	
	Fresh solution	Aged solution[d]
100^a	32.74	
94.88	30.71^c	
75.1	22.0	21.9
60.8	15.2	
50.0	10.0	9.9
40.1	3.5	3.2
24.5	-7.2^c	-7.2^c
7.87	−29.9	
7.3^e	-39.7^e	
6.83	−39.6	
3.79	−38.46	
2.89	−38.13	
1.83	−37.70	
0^b	−36.92	

[a] Dichlor 99.42 mole %. [b] Difluor 99.72 mole % purity. [c] Melting point. [d] Solutions aged one week at room temperature. [e] Eutectic composition, extrapolated.

The ideality exhibited by dichlor–difluor solutions and the absence of a solid third component do not in themselves rule out the existence of significant amounts of a third component in solu-

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(19) G. T. Furukawa, M. L. Reilly and J. M. Henning report in preparation for publication in *J. Res Natl. Bur. Standards.*

(20) The Clausius–Clapeyron equation may be written $\ln N_1 = C\Delta T/T_1$. C being $-L_f/RT_0$, where N_1 is the mole fraction of solvent, ΔT is the freezing point depression, T_1 and T_0 are the freezing points of the solution and solvent, respectively, R, is the gas constant and L_f is the latent heat of fusion of the solvent.

(21) Furukawa, *et al.*,[15] obtained 4.32 and 2.84 kcal./mole for dichlor and difluor, respectively, by direct measurement with purified samples.

tion. However, if chlorfluor were formed in the binary mixture, the freezing point depressions would be greater than in cases where ideal nonreactive solutes were added to either component. Carefully prepared solutions of 25 mole % benzene in dichlor and 2 mole % benzene in difluor gave freezing point depressions within 1.5% of the values calculated from the heats of fusion of the solvents.

Infrared Spectra.—The 2 to 15 μ region of the infrared spectra of dichlor,[22,23] difluor, chlorfluor and an equimolar solution of dichlor and difluor were obtained initially with a Perkin–Elmer Model 12-C Spectrometer equipped with a NaCl prism. Measurements in the 2 to 15 μ region spectra were later repeated, and the spectral range extended to 25 μ by the use of Perkin-Elmer Model 21 Spectrophotometers equipped with NaCl and KBr prisms. Spectra from 2–12 and 14–25 μ were obtained in CCl_4 solutions. In the 12 to 14 μ region use was made of CS_2 solutions or capillary films. The spectrum of the equimolar dichlor–difluor mixture was found to consist of the additive absorptions of the components, no new bands being observed. The spectrum of chlorfluor was found to be sufficiently different from that of the dichlor–difluor solution to make certain estimations possible. The spectra will be presented and discussed more fully in a separate publication.[24]

The infrared spectra were used to estimate the extent of metathesis in an aged equimolar dichlor–difluor solution and of disproportionation in an aged sample of chlorfluor.

For the first purpose, the sensitivity of the identification of chlorfluor in an equimolar solution of dichlor and difluor was determined by spectral examination of a freshly-prepared equimolar solution to which was added 8.2 mole % chlorfluor. Calculations based on the spectrum of this reference mixture indicated that as little as 2 mole % chlorfluor would be detectable in the mixture due to increased absorption at 7.55 μ. The spectrum of the reference mixture (compared with 50–50 dichlor–difluor) also showed increased absorption at 7.75 and 23.65 and decreased absorption at 10.56 and 11.38 μ, but the magnitudes of these changes were somewhat less than at 7.55 μ.

Spectra of the freshly-prepared equimolar dichlor–difluor mixture, and of a similar mixture that had been stored in glass at room temperatures for over six months showed no differences at the significant wave lengths, indicating that less than 1 mole % each of dichlor and difluor had metathesized to chlorfluor.

For the estimation of disproportionation of aged chlorfluor, a strong absorption band of dichlor at 20.16 μ and of difluor at 21.28 μ were examined. These bands are completely free of interference due to chlorfluor and do not overlap, making it possible to estimate dichlor and difluor to 1.5 and 1.0 mole %, respectively, in chlorfluor.

The aged sample of chlorfluor examined had been purified originally (by crystallization) to 99.7 mole % and had been stored in a glass ampoule for 34 months at room temperature. This particular sample had not been examined by infrared prior to storage, but other samples of chlorfluor have shown small amounts of dichlor and difluor immediately after distillation. The infrared estimations of the dichlor and difluor contents of this aged chlorfluor were 4.0 and 4.8 mole %, respectively. An assumed value for the transmittance of chlorfluor containing no disproportionation products was employed for these estimates, since no data were available for the completely pure compound.

Metathesis of Dichlor–Difluor Solutions.—Study of the physical properties, phase relations and infrared spectra that were measured on dichlor, difluor, chlorfluor and dichlor–difluor mixtures indicated that the equilibrium constant of metathesis (reaction 6) is very small or that equilibrium is extremely slow of attainment, or both.

Refluxing an equimolar dichlor–difluor solution at 133° (the normal boiling point) for 16 hr. resulted in a freezing point depression of only 1.2°, corresponding to the formation of about 2 mole % of an ideal impurity. It will be shown later that this is approximately the equilibrium concentration of chlorfluor at the reflux temperature. We have shown that the freezing points of dichlor–difluor mixtures (Table III) do not change appreciably after a week at room temperature. Hoffmann[7] gives data indicating approximately 16% disproportionation of a somewhat impure sample of chlorfluor in 70 hr. at 60° and has distilled the compound at its normal boiling point (126°) without appreciable disproportionation.

The 99.7 mole % sample of chlorfluor stored in a glass ampoule for 34 months at ambient temperatures showed a freezing point rise of 0.18°. The close agreement between the freezing and melting points of this sample (f.p. 0.017° lower than m.p.) appears to preclude the existence of solid solutions here. When small amounts of equimolar dichlor–difluor solution were added to this aged chlorfluor, the freezing point again was elevated. It is possible that sufficient disproportionation had occurred during the 34 months at ambient temperature to place the resulting composition in a phase area of the ternary system in which the chlorfluor is the solute rather than the solvent. The phase diagram of the ternary system was not studied since infrared examination indicated the extent of disproportionation to have been slight.

In order to obtain quantitative information on the position of equilibrium in reaction 6, Furukawa, *et al.*,[19] and Prosen[19] measured the low-temperature heat capacities and heats of reaction for the methylphosphonic dihalides and computed the enthalpies, entropies and free energies of formation of these compounds.

Using the thermodynamic relationship $\Delta F = -RT \ln K$, the equilibrium constant of reaction 6 was calculated over the temperature range 25–125° using extrapolations above 50°. The results are in Table IV.

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(22) R. A. McIvor, G. A. Grant and C. E. Hubley, *Can. J. Chem.*, **34**, 1611 (1956).

(23) H. Gording and H. W. Maarsen, *Rec. trav. chim.*, **76**, 481 (1957).

(24) J. B. Bouck, paper in preparation.

(25) E. J. Prosen, report in prepn. for publication in *J. Res. Natl. Bur. Standards*.

TABLE IV

EQUILIBRIUM CONSTANTS OF METATHESIS

Temp., °C.	Equil. const. × 10⁴	Concn. chlorfluor at equil., mole %
25	1.69	0.65
50	4.05	1.0
75	7.14	1.3
100	11.4	1.7
125	16.4	2.1

Thus, it is shown that not only is the attainment of equilibrium in reaction 6 slow, but metathesis at equilibrium amounts only to about 0.7 mole % at 25°.

Esterification of Methylphosphonic Halides.—The relative esterification rates of methylphosphonic halides in 2-propanol solution, obtained by heat evolution measurements, are in the order: chlorfluor $\gg$ dichlor $>$ equimolar dichlor–difluor mixture $\gg$ isopropyl methylphosphonic chloride $>$ difluor. The esterification of difluor is catalyzed by acids, whereas that of isopropyl methylphosphonic chloride is not. When a mole of 2-propanol was added to a mixture containing a mole each of dichlor, difluor and chlorfluor, a mole of Sarin was produced and the original quantities (within 5%) of dichlor and difluor were recovered by distillation. This indicates the rapidity of chlorfluor reaction relative to the other dihalides and also that neither HF, HCl nor 2-propanol catalyzes the disproportionation of chlorfluor.

In considering the mechanism of esterification of an equimolar mixture (dichlor–difluor), it can be seen that the small equilibrium amounts of chlorfluor that might be present would react first. The only remaining question concerning the participation of chlorfluor in the mechanism is whether attainment of equilibrium in reaction 6 is sufficiently rapid to replenish the supply of chlorfluor reacting.

The esterification of the dichlor–difluor mixture is essentially complete within 30 minutes at 25°. The metathesis of this mixture to chlorfluor would have to be at least as rapid for the alcohol to react to any significant degree with chlorfluor. Because of the small equilibrium constant of metathesis ($K = 1.7 \times 10^{-4}$), the rate could not be measured conveniently. Since the reverse reaction, disproportionation of chlorfluor, should theoretically go almost to completion and is 6000-fold more rapid at equivalent concentrations, it can be followed. The slow change reported by Hoffmann at 60° and the slight changes indicated in the freezing point and infrared spectrum of chlorfluor during 34 months of storage at room temperature attest to the relative unimportance of chlorfluor participation in the mechanism studied.

The relative rate data obtained tend to substantially confirm the Sarin formation mechanism postulated by Perry.

Grateful acknowledgment is given to Mr. J. B. Bouck of these Laboratories for making available to us for discussion the results of the infrared measurements prior to his more detailed publication.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, NEW YORK]

Structural Studies of Ribonuclease. III. A Model for the Secondary and Tertiary Structure[1,2]

BY HAROLD A. SCHERAGA

RECEIVED SEPTEMBER 8, 1959

A three-dimensional model of ribonuclease has been constructed on the basis of available data on the primary, secondary and tertiary structure. The model will be useful for the design of future experiments to establish the complete structure of this protein.

In the previous papers of this series[3,4] information was obtained about the internal hydrogen bonding in ribonuclease. With the recent availability of the complete amino acid sequence of oxidized ribonuclease[5] and the location of the disulfide bridges in the native molecule,[6] it is now possible to construct a model of ribonuclease which will be consistent with the available data on the primary, secondary and tertiary structure. It must be emphasized at the outset that the model to be described here may not necessarily be a unique one. However, it is believed to be consistent with the known structural information about this protein and, further, it provides a basis for future experiments to prove the presence or absence of interactions between specific side-chain groups. Presumably the complete three-dimensional structure of ribonuclease will be established when a sufficient number of such interactions is located.

Model Building Units.—A description of the Pauling–Corey model building units, and the molecular dimensions on which they are based, has already been presented by Lindley and Rollett in their paper on the structure of insulin.[7] I am indebted to Dr. R. B. Corey for sending me blue-

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(2) Presented before the Division of Biological Chemistry at the 136th meeting of the American Chemical Society, Atlantic City, New Jersey, September, 1959.

(3) C. Y. Cha and H. A. Scheraga, THIS JOURNAL, **82**, 54 (1960).

(4) C. L. Schildkraut and H. A. Scheraga, *ibid.*, **82**, 58 (1960).

(5) C. H. W. Hirs, S. Moore and W. H. Stein, *J. Biol. Chem.*, **235**, 633 (1960). I am indebted to Dr. Hirs for sending me a copy of the sequence prior to publication.

(6) D. H. Spackman, W. H. Stein and S. Moore, *ibid.*, **235**, 648 (1960).

(7) H. Lindley and J. S. Rollett, *Biochim. et Biophys. Acta*, **18**, 183 (1955).