142.0°. The acid phthalate obtained from this salt was recrystallized to constant rotation from ether–pentane mixtures. This material had $[\alpha]^{25}_{D}$ −266 ± 2° ($CHCl_3$), lit.[7] $[\alpha]^{25}_{D}$ −130.4° ($CHCl_3$), and was shown to be optically pure (see below).

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20; neut. equiv., 260.3. Found: C, 69.14; H, 6.20; neut. equiv., 260.7.

Saponification of the acid phthalate with 2.5 *M* sodium hydroxide[7] gave optically pure (−)-*trans*-5-methyl-2-cyclohexenol, $[\alpha]^{23}_{D}$ −265° (neat). This alcohol was converted to optically pure (−)-*trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoate, m.p. 70–71°, $[\alpha]^{25}_{D}$ −295.3° (*c* 0.98, acetone).

Carbonyl-O^{18} IV was prepared from the pure alcohol and carbonyl-O^{18} *p*-nitrobenzoyl chloride.[5a]

Determination of Optical Purity of (−)-*trans*-5-Methyl-2-cyclohexenyl Acid Phthalate.—The optical purity of the acid phthalate described above was established by a modification of the isotope dilution method described by Berson and Ben-Efraim.[8]

dl-trans-5-Methyl-2-cyclohexenyl acid phthalate-7-C^{14} was prepared from pure *trans*-alcohol and phthalic anhydride-7-C^{14} (Tracerlab Inc.). After purification by recrystallization (ether–pentane mixtures) this material gave a correct carbon and hydrogen analysis, melted at 89–91° and had 68,200 ± 300 d.p.m.[12]

A mixture of 1.4954 g. of (−)-acid phthalate, $[\alpha]^{25}_{D}$ −265.2°($CHCl_3$), and 0.7004 g. of radioactive *dl*-acid phthalate was dissolved in 15 ml. of acetone containing 3.368 g. of brucine. The brucine salt was recrystallized five times and the recovered acid phthalate was then recrystallized from ether–pentane until optically pure; *i.e.*, $[\alpha]^{25}_{D}$ −265.9° ($CHCl_3$). The radioactivity of the optically pure sample was 12,980 ± 90 d.p.m. From these data it can be determined[8] that optically pure (−)-acid phthalate has $[\alpha]^{25}_{D}$ −265 ± 2° ($CHCl_3$).

Polarimetric and Titrimetric Rates.—The ampule technique[3,4] was used to obtain k_α and k_t. For the polarimetric runs aliquots (in ampules) were stored at 10° and then rotations on successive aliquots were determined at 25 ± 1°. A 4-dm. polarimeter tube equipped with central tubulation for filling was used to determine the rotations and the end-plates of the polarimeter tube were not removed during a kinetic experiment. The total change in optical rotation during a run was about 2–3°.

Determination of O^{18} Equilibration in *dl-trans*-5-Methyl-2-cyclohexenyl *p*-Nitrobenzoate-carbonyl-O^{18}.—Solutions (0.05 *M*) of *dl-trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoate in 60 or 80% aqueous acetone were sealed in glass bombs of 200-ml. capacity and placed in a constant temperature oil-bath at 100°. The progress of the reaction was followed polarimetrically and titrimetrically.

In experiment 12, Table II, the solution of the ester (6.723 g.) dissolved in 500 cc. of 80% aqueous acetone (0.0519 *M*) was distributed in three sealed glass bombs and heated at 99.65 ± 0.02°. One bomb was removed from the bath after 41.8 hours and the remaining two after 80.3 hours. Each point was treated as follows: The *p*-nitrobenzoic acid produced by solvolysis was neutralized with sodium hydroxide and the acetone was evaporated from the cold solution at *ca.* 15 mm. pressure. The ester and solvolysis products were extracted with diethyl ether and dried over magnesium sulfate. The ether was evaporated and the ester was purified by extensive evacuation over calcium chloride (sometimes including 30-min. to 2-hour heating at 50° or treatment of an ethereal solution with calcium chloride) and recrystallization from ether–pentane. In all cases the infrared spectra corresponded to that of pure *trans* *p*-nitrobenzoate and showed that the samples were not contaminated with alcohol.

The ester was saponified by refluxing 2 hours in methanolic potassium hydroxide (18 ml. of methanol containing 1 g. of KOH per gram of ester). The methanolic solution was diluted with an equal volume of water and the resulting solution was extracted continuously with pentane for 40 hours. The resulting alcohol was converted to its *p*-nitrobenzoate derivative for O^{18} analysis.[5a] The results of three experiments are shown in Table II.

Control experiments which demonstrate that isolation, saponification and derivatization are not accompanied by rearrangement or exchange or in other words that the O^{18} content of the *p*-nitrobenzoate derivative corresponds to that of the ether-oxygen atom of the unsolvolyzed IV in the reaction mixture have been outlined in a preceding section.

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[12] The d.p.m. reported is per millimole of compound and has been corrected for background and efficiency of the counting. The C^{14} contents were determined with a Packard Tri-Carb liquid scintillation spectrometer model 314-DC (toluene–2,5-diphenyloxazole solution). We are indebted to Professor C. Heidelberger, University of Wisconsin, for making these facilities available to us.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE DOW CORNING CORPORATION, MIDLAND, MICH.]

Inductive Effects in the Chlorosilane Hydrolysis Equilibrium[1]

BY J. F. HYDE, P. L. BROWN AND A. LEE SMITH

RECEIVED JUNE 13, 1960

A detailed study of a series of nine triorganosubstituted chlorosilanes has shown that their hydrolysis involves a readily reversible equilibrium which intimately relates chlorosilane and siloxane chemistry. Free energy changes and heat of reaction values which are important to basic understanding of organosilicon chemistry have been derived. Marked changes in the equilibrium constants are brought about by changes in the substituent organic groups. These differences arise from inductive effects transmitted through the central silicon atom to modify the chemical reactivity of the electron-rich chlorine atom. Supporting this interpretation is the good correlation obtained between the equilibrium constants and the infrared frequency shift of the SiH vibration for the corresponding silane, which is also determined by the inductive effect of the organic substituents. This direct correlation of the chemical reactivity with precise infrared measurements offers a new approach to equilibrium studies and to the calculation of important thermodynamic data not previously available.

Introduction

The organochlorosilanes constitute one of the most important classes of compounds in the organosilicon field since they are intermediates from which industrial silicones are made.

One of the most striking and characteristic reactions of chlorosilanes is their rapid hydrolysis to produce hydrogen chloride and silanols, siloxanes, or both, depending upon the conditions imposed during the hydrolysis reaction.

It is generally recognized on a qualitative basis that the readiness with which hydrolysis occurs, under comparable conditions, is noticeably influenced by the degree of organic substitution, as shown by the series in decreasing order: $SiCl_4 > RSiCl_3 > R_2SiCl_2 > R_3SiCl$.

A basic understanding of such hydrolysis phenomena is of great interest and importance from an academic as well as industrial point of view.

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[1] Presented in part before the Organic Division of the American Chemical Society at the 136th National Meeting at Atlantic City, N. J., September 13–18, 1959.

General Discussion

A detailed study of the R_3SiCl-type compounds has shown that a readily reversible equilibrium is involved in the hydrolysis reaction, in accordance with the equation

$$R_3SiCl + H_2O \rightleftharpoons (R_3Si)_2O + HCl \qquad (1)$$

The reverse reaction represents an important reaction of the disiloxanes, namely, their ability as bases to react with hydrochloric acid and form the chlorosilanes.[2] Although silanols might be expected to be involved in the reaction, no detectable amounts have been found under equilibrium conditions.

It is important to consider that a heterogeneous system is involved in the equilibrium. In general, the organosilicon compounds and water are mutually soluble to the extent of less than 0.1%. Thus the activities of the water and hydrochloric acid are controlled in the system by the aqueous phase concentrations. Since thermodynamic data on the system HCl-H_2O are readily available,[3] a direct study of the equilibrium reaction was therefore possible.

The experimental method, accordingly, consisted of mixing appropriate amounts of the siloxane, chlorosilane, water and aqueous HCl to give the desired acid concentration range and bringing the mixture to equilibrium at 25° with suitable agitation. The two phases were carefully separated, sampled and titrated to determine the aqueous acid concentration as well as the chlorosilane content of the siloxane phase.

In addition to the equilibrium studies on various organosubstituted chlorosilanes at 25°, the trimethyl system was examined at 10°, 25° and 45° in order to obtain the temperature coefficient of the equilibrium constant and thus derive the value of ΔH for this system.

Extensive density-composition studies of the chlorosilane–siloxane mixtures were made to obtain appropriate volume concentration data. A linear plot of the reciprocal of densities against compositions gave straight lines, showing that no unusual solubility effects were present.

Standard equations were used in calculating the thermodynamic equilibrium constants and corresponding molal free energy changes.[4]

Interpretation of Results

The values of the equilibrium constants and the molal free energy changes in calories are given in Table I. One result immediately apparent is the 500-fold increase in the constant with change in the nature of the groups in going down the table. There is an accompanying systematic variation of 3700 calories in the values of the free energy change.

The data pertinent to determining the temperature coefficient of the equilibrium constant for the trimethyl system are presented in Table II. It is important here to observe that the constant is decreasing with increasing temperature. Thus, the tendency to hydrolyze is favored by decreasing temperature. The value of ΔH at 25° as determined from these data is −24,000 cal./mole (see Fig. 1).

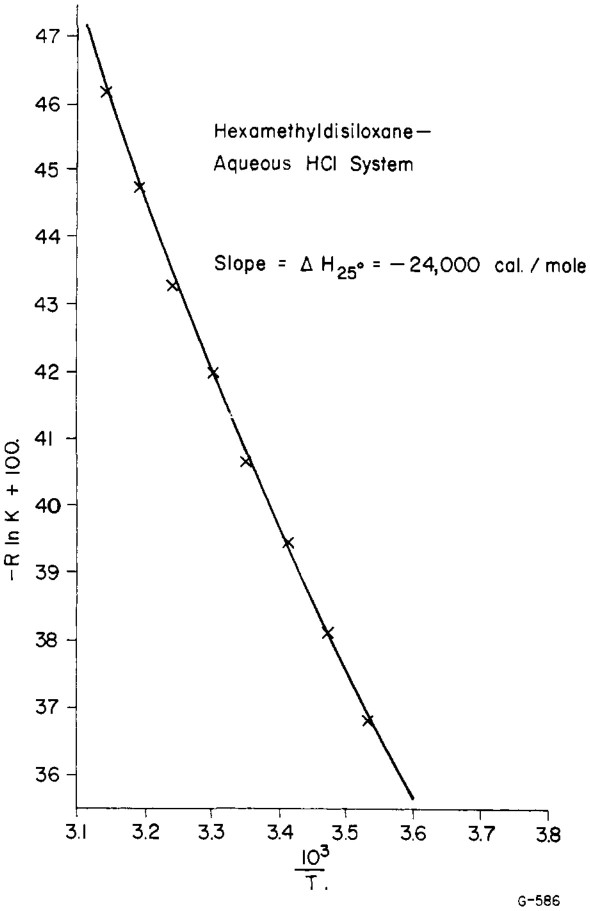

Fig. 1.—Graphical determination of the heat of reaction for the hexamethyldisiloxane–trimethylchlorosilane system.

TABLE I

EQUILIBRIUM CONSTANTS

Chlorosilane	$K^{25°} \times 10^{-11}$	$\Delta F^{25°}$
Et_3SiCl	3.5	−15,700
$EtMe_2SiCl$	28.8	−17,000
Me_3SiCl	91.0	−17,700
$F_3C(CH_2)_2Me_2SiCl$	150	−17,900
$Me_2PhSiCl$	204	−18,100
$Me_2ViSiCl$	240	−18,200
$MePhViSiCl$	446	−18,600
Cl_2PhMe_2SiCl	709	−18,900
$ClCH_2Me_2SiCl$	1800	−19,400

TABLE II

VARIATION OF THE EQUILIBRIUM CONSTANT WITH TEMPERATURE FOR THE SYSTEM Me_3SiCl–$(Me_2Si)_2O$

Temp., °C.	$K \times 10^{-12}$	ΔF	Temp., °C.	$K \times 10^{-12}$	ΔF
10	61.0	−17,900	30	4.60	−17,600
15	33.0	−17,800	35	2.30	−17,400
20	17.6	−17,700	40	1.10	−17,300
25	9.10	−17,700	45	0.57	−17,100

Since we are examining systems at equilibrium, reactive intermediates, mechanism and other factors involved in reaction kinetics do not influence the interpretation of the present data.

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[2] J. F. Hyde, U. S. Patent 2,615,034 (1952).

[3] G. Åkerlöf and J. W. Teare, THIS JOURNAL, 59, 1855 (1937).

[4] G. N. Lewis and M. Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., 1923.

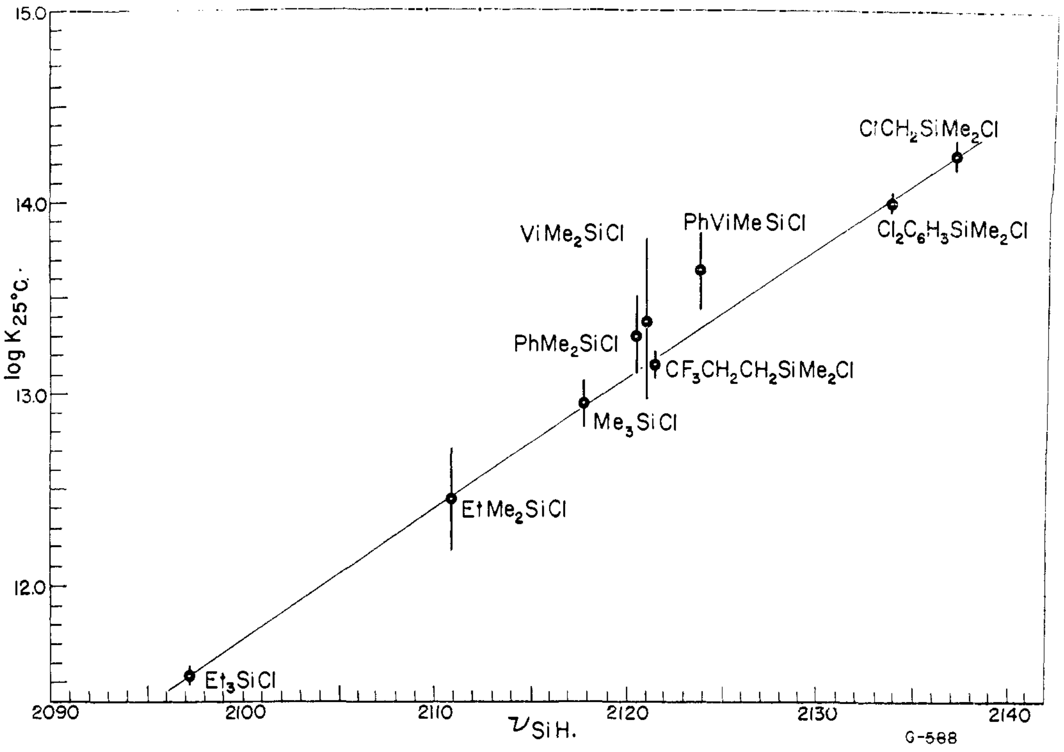

Fig. 2.—Relationship between the equilibrium constants for hydrolysis of chlorosilanes and the infrared frequency shift for the SiH vibration in the corresponding hydrosilanes.

The marked effect of the nature of the groups on the value of the equilibrium constants does not appear to correlate with the bulkiness of the groups. This observation can be verified by comparing, for example, the triethyl-, trimethyl-, dichlorophenyldimethyl- and the chloromethyldimethyl- compounds. An examination of Hirschfelder–Taylor models for the chlorosilanes and disiloxanes supports the belief that bulk steric effects must be of minor importance.

One variable factor, which becomes apparent on examining the compounds involved, is the considerable variation in electronic content of the attached groups.

It is to be expected that polarizing effects due to variations in electronic character of the component atoms will be distributed throughout the molecule in some pattern consistent with the energy distribution requirements of the molecule and in a manner characteristic of the molecule in question.

On this basis, the change in equilibrium constant with change in groups is a measure of these integrated polarizing effects on the reactivity of the silicon–chlorine and silicon–oxygen bonds which are transmitted through the central silicon atom.

Correlation with Infrared Data

In a recent publication, Smith and Angelotti[5] have shown that the frequency of the SiH stretching absorption in substituted silanes varies with the substituents. Furthermore, each substituent makes a definite contribution to the shift and, from a table giving characteristic constants (E-values) for each possible substituent, one can calculate quite accurately the SiH frequency for any substituted silane. Since the effect is reproducible and additive for a great many molecules, it must arise from the inductive effect of the substituents. Thomson,[6] in fact, has correlated these constants with the inductive parameter σ^* proposed by Taft.[7]

The SiH stretching frequency of the trisubstituted silanes correlates well with the logarithm of the equilibrium constant for the hydrolysis of the corresponding chlorosilane, as shown in Fig. 2. Although not all the points fall on the line, the discrepancy is probably due to experimental error in the determination of the equilibrium constants. The magnitude of these errors has been calculated statistically from the spread in the experimental values. The maximum variation for log K, using a 99% confidence limit (3 σ), is given by vertical lines at each point in Fig. 2, and in all but one case overlap the correlation line. This exception may be due to cleavage of small amounts of phenyl and vinyl groups under the conditions of the experiment. The correlation shown in Fig. 2 opens up a vast field of unexplored thermodynamic data which can be calculated from the infrared results, equilibrium constants thus may be calculated from the equation

$$\log K\ (25°) = 0.006826\Sigma E - 131.63 \qquad (2)$$

where ΣE represents the sum of the three E-values for the silicon substituents. Table III gives a compilation of these constants. It is interesting that log K does not correlate as well with Taft's σ^* as with the E-values given.

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(5) A. L. Smith and N. C. Angelotti, *Spectrochim. Acta*, **15**, 412 (1959).

(6) H. W. Thomson, *ibid.*, 238 (1960).

(7) R. W. Taft, THIS JOURNAL, **74**, 3120 (1952); **75**, 4231 (1953).

TABLE III

Group	E-Value	Group	E-Value
OAc	762.1	C_6H_5	708.7
F	760.8	$CF_3(CH_2)_3$	708.7
Cl	752.8	$C_6H_5CH_2$	706.5
Br	745.3	$CH_2{=}CHCH_2$	706.4
OMe	734.4	Me	705.9
OEt	732.0	n-Pr	700.1
$C_6H_5C{\equiv}C$	731.0	n-Bu	700.1
2-EtBuO	730.4	n-C_5H_{11}	700.1
O-iPr	730.3	n-C_6H_{13}	700.1
CH_2Cl	725.3	Et	699.1
H	724.8	$C_6H_5CH_2CH_2$	699.0
p-C_6H_4Cl	714.0	t-Bu	696.5
m-C_6H_4Cl	711.3	i-Pr	694.3
$CF_3(CH_2)_2$	709.7	Cyclo-C_6H_{11}	691.5

$$\nu\text{SiH} = \sum_3 E_i$$

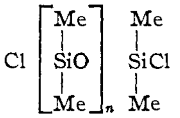
Table IV gives calculated K values for the hydrolysis of a number of typical chlorosilanes.

TABLE IV

CALCULATED K'S FOR VARIOUS CHLOROSILANES

Molecule	E	K (calcd.)	ΔF (25°) (calcd.), cal./mole
ClSiCl$_3$	2258.3	3.3×10^{22}	−30,700
ClSiMeCl$_2$	2211.5	2.1×10^{19}	−26,350
ClSiPh$_2$Cl	2170.2	3.1×10^{16}	−22,480
ClSiMeViCl	2167.9	2.2×10^{15}	−22,280
ClSiVi$_3$	2127.6	4.0×10^{13}	−18,550
ClSiPh$_3$	2126.0	3.1×10^{13}	−18,400
ClSi(nPr)$_3$	2100.3	5.5×10^{11}	−16,010

Brown, *et al.*,[8] have determined the equilibrium constant for the hydrolysis of dimethyldichlorosilane as $K = 1.74 \times 10^{14}$. Since the polymer sizes vary according to a statistical distribution pattern, the method given here cannot be used to calculate the equilibrium constant exactly. It can, however, be bracketed for the limiting cases of a disiloxane and an essentially infinite siloxane chain. For the polymer



$$Cl\left[\begin{array}{c}Me\\ |\\ SiO\\ |\\ Me\end{array}\right]_n \begin{array}{c}Me\\ |\\ SiCl\\ |\\ Me\end{array}$$

if $n = 1$, $\Sigma E = 2173.6$ and $K = 5.5 \times 10^{16}$. If $n = \infty$, $\Sigma E = 2126.7$ and $K = 3.5 \times 10^{13}$. The observed value, $K = 1.74 \times 10^{14}$, falls in between the predicted limits.

The good correlation between the equilibrium constants and the infrared data further confirms the belief that the major effect in the hydrolysis equilibrium is inductive, with increased electron concentration around the central silicon atom acting to promote replacement of the electron-rich chlorine atom by oxygen.

Experimental

Materials.—The chlorosilanes and disiloxanes were freshly redistilled for use in this work. The chloro-2,5-dichlorophenyldimethylsilane boiled at 100° (2 mm.) and the corresponding disiloxane boiled at 182.5° (2 mm.). The other chlorosilanes agreed well with properties described in the literature: triethylchlorosilane,[9] ethyldimethylchlorosilane,[10] trimethylchlorosilane,[11] dimethyl-γ-trifluoropropylchlorosilane,[12] dimethylphenylchlorosilane,[13] dimethylvinylchlorosilane,[14] methylphenylvinylchlorosilane[15] and dimethylchloromethylchlorosilane.[16]

Methods.—The equilibrations were carried out by mixing the aqueous and siloxane phases with shaking in a glass tube equipped with a stopcock and capillary tube on each end. The vessels held approximately 40 ml. and were of such a weight that they were within the capacity of an analytical balance. The general mechanics of the method consisted of filling the reactor tube approximately one-third full with chlorosilane, disiloxane or a mixture, and then adding approximately an equal volume of aqueous HCl. The strength of the acid was varied depending upon the make-up of the siloxane layer to give the final aqueous acid concentration desired. Final acid concentrations of over 36.5% could be obtained by adjustment of the chlorosilane concentration. The mixtures were shaken for 16 hours or more by a Wrist-Action Shaker at room temperature of 23–25°. The 25° equilibrium was finally obtained by immersion in a thermostat for 3–5 hours more with intermittent shaking. Secondary reactions involving cleavage of vinyl and phenyl groups were minimized by avoiding excessive reaction times and working in the lower range of acid concentrations. The $(Me_3Si)_2O$–Me_3SiCl equilibrations were also carried out in a larger thermostated 2-gallon glass-lined reactor with results in good agreement with those from the small glass device.

Analysis.—After equilibration, samples of the aqueous phase were weighed directly from the reactor tube and titrated with 0.25 N NaOH using phenolphthalein as indicator to determine the concentration of acid. In some cases, with higher acid concentrations in the 2-gallon reactor under some pressure, sampling was done by running the aqueous acid sample directly into a weighed amount of standard NaOH, weighing again and then determining the excess alkali by back-titration.

The siloxane–chlorosilane phase was then sampled for infrared analysis. This phase was then placed under a slightly reduced pressure to remove any dissolved HCl gas. Extreme care was taken in this step to avoid removal of low boiling chlorosilanes. A sample of this degassed siloxane–chlorosilane mixture was weighed into a solution of toluene–butanol and the resulting HCl formed from the hydrolysis of the chlorosilane was titrated with standard alcoholic KOH using brom cresol purple as indicator. The amount of this HCl was used to calculate the weight per cent. of chlorosilane in the equilibrated siloxane–chlorosilane mixtures.

A series of 8 to 12 determinations was made for each chlorosilane at various acid concentrations in the range of 26–43%. By plotting on semilog paper the weight per cent. of chlorosilane against per cent. HCl as the linear function, a series of essentially parallel curves was obtained from which smoothed values relating the concentrations of HCl and chlorosilane were derived.

Density Studies.—Standard pycnometers were used to determine densities and determinations were all made at 25°. A series of 6 to 8 mixtures of varying chlorosilane content was measured for each system and the resulting densities were plotted linearly against per cent. chlorosilane. These density data, along with the concentration data previously mentioned, were used for calculation of concentration in terms of moles per liter.

Thermodynamic Properties of Aqueous HCl.—The activity values for HCl and H_2O in the aqueous phase used in the calculation of the constants were taken from the data of Åkerlöf and Teare[3] in the range 10 to 16 molal, and from graphical extrapolation of their data to 21 molal.

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(8) P. Brown, E. Schultz, J. F. Hyde and L. B. Bruner, unpublished work.

(9) A. Ladenburg, *Ann.*, **164**, 325 (1872); P. A. DeGiorgio, W. A. Strong, L. H. Sommer and F. C. Whitmore, THIS JOURNAL, **68**, 1380 (1946).

(10) F. C. Whitmore, L. H. Sommer and J. Gold, *ibid.*, **69**, 1976 (1947).

(11) R. R. McGregor and E. L. Warrick, U. S. Patent 2,386,488 (1945); D. T. Hurd, THIS JOURNAL, **67**, 1545 (1945).

(12) O. W. Steward and O. R. Pierce, *ibid.*, **81**, 1983 (1959).

(13) R. N. Lewis, *ibid.*, **70**, 1115 (1948); W. H. Daudt and J. F. Hyde, *ibid.*, **74**, 386 (1952).

(14) J. Curry, *ibid.*, **78**, 1686 (1956).

(15) J. Curry, *ibid.*, **78**, 1686 (1956).

(16) J. J. McBride and H. C. Beachell, *ibid.*, **70**, 2532 (1948).

TABLE V

TYPICAL DATA FOR THE Me_3SiCl–$Me_3SiOSiMe_3$ EQUILIBRIUM AT 25°

m	HCl %	a_1	a_2	A	B	10^{-12} K
10	26.72	0.4246	11,000	0.01511	4.674	10.4
12	30.50	.3224	44,500	.08327	4.631	9.7
14	33.80	.2426	152,000	.3385	4.478	9.6
16	36.82	.1821	438,000	1.148	3.992	7.9
18	39.68	.1349	1,130,000	3.540	2.568	8.3
20	42.20	.0988	2,610,000	6.471	0.8255	9.6

The extrapolated values agree well with values calculated from the equations of these authors. There is admittedly some risk of error in such an extrapolation, but the equilibrium constants are relatively insensitive to small changes in HCl activity, and the K's obtained showed no systematic dependence on HCl concentration. Data obtained from a typical series of determinations are shown in Table V.

Calculation of Equilibrium Constants.—Equilibrium constants were calculated from eq. 3

$$K = \left[\frac{B}{A + B}\right] a_2^2 \Big/ \left[\frac{A}{A + B}\right]^2 a_1 = \frac{B[A + B]a_2^2}{[A]^2 a_1} \quad (3)$$

$$\Delta F = -RT \ln K \quad (4)$$

where

A = moles/liter of R_3SiCl
B = moles/liter of $(R_3Si)_2O$
a_1 = activity of H_2O
a_2 = activity of HCl
K = equilibrium constant
ΔF = molal free energy change
m = molality of the HCl

Determination of ΔH for the Me_3SiCl–$(Me_3Si)_2O$ system.—The result of plotting $100 - R \ln K$ linearly against $1/T$ is shown in Fig. 1, where the slope of the curve at 25° gives ΔH = 24,000 cal./mole.

Acknowledgment.—The authors wish to acknowledge the help of Elmer Schultz and Leonard Bruner in carrying out the work.

[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, THE JOHNS HOPKINS SCHOOL OF MEDICINE, BALTIMORE 5, MD.]

The Effect of Geminal Substitution Ring Size and Rotamer Distribution on the Intramolecular Nucleophilic Catalysis of the Hydrolysis of Monophenyl Esters of Dibasic Acids and the Solvolysis of the Intermediate Anhydrides

BY THOMAS C. BRUICE[1a] AND UPENDRA K. PANDIT[1b]

RECEIVED APRIL 7, 1960

The intramolecular nucleophilic catalysis of ester hydrolysis by the carboxyl group of monoesters of dicarboxylic acids (*i.e.*, monoester → cyclic anhydride → dibasic acid) has been investigated in regard to the kinetic effects of geminal substitution, ring size and conformation of the carbophenoxy and carboxyl groups. α,α-Dimethyl substitution in both the monosuccinate and glutarate esters brings about an almost identical rare enhancement in anhydride formation. In the glutarate monoester β,β-dimethyl substitution is more effective than α,α-dimethyl substitution in increasing the rate of anhydride formation. The increase in rate of anhydride formation brought about by geminal substitution has been explained on the basis of a decrease in unprofitable rotamer distribution in the ground state. When the nucleophilic carboxyl group is held rigidly in an eclipsed position to the carbophenoxy group the expected large rate enhancement in the formation of anhydride is noted. Succinate monoesters form anhydrides 230 times as fast as the corresponding glutarate esters because of a decrease in the effective distance between the reacting groups, whereas the resultant anhydrides have similar solvolysis rate constants. These results have been explained on the basis that the rate-determining step in each case is the initial nucleophilic attack. The various types of geminal substitution decrease the rates of anhydride solvolysis. Since the rate-determining step in the latter reaction is the attack of lyate species, the kinetically negative effect of geminal substitution is ascribed to the steric hindrance to approach of the nucleophile. Though one or two β-substituents increase the rate of glutaric anhydride formation, only β,β-disubstitution hinders anhydride solvolysis. The existence of one bulky substituent in the equatorial position in the cyclic anhydride explains the lack of steric hindrance to the approach of a nucleophile while in the alicyclic ester a single β-substituent can hinder the rotation of reacting groups away from each other and thus influence the rate.

Introduction

The phenomenon of bimolecular nucleophilic catalysis[2] of ester hydrolysis was first recognized by Bender and Turnquest[3] and by Bruice and Schmir[4] in their studies of the catalysis of phenyl acetate(s) hydrolysis by the nitrogen bases imidazole,[3,4] substituted imidazoles[5] and pyridines.[4,5] The phenomenon has since been treated as a special case of nucleophilic displacement at the ester carbonyl group.[6,7] The intramolecular nucleophilic catalysis of the hydrolysis of the ester bond has been investigated by Garrett,[8] Morawetz,[9,10] Bender[11,12] and Bruice[13-16] and co-workers, and has received particular attention because of its apparent similarity to enzymic catalysis.[17]

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[1] (a) Department of Chemistry, Cornell University, Ithaca, New York. (b) Postdoctoral Research Fellow, Department of Physiological Chemistry, The Johns Hopkins School of Medicine.

[2] Bimolecular nucleophilic catalysis of ester hydrolysis is that process in which a nucleophile replaces -OR' from R-CO-OR' to yield an intermediate whose rate of formation and hydrolysis is greater than the rate of solvolysis of R-CO-OR'.

[3] M. L. Bender and B. W. Turnquest, THIS JOURNAL, **79**, 1656 (1957).

[4] T. C. Bruice and G. L. Schmir, *ibid.*, **79**, 1663 (1957); *Arch. Biochem. & Biophys.*, **63**, 484 (1956).

[5] T. C. Bruice and G. L. Schmir, THIS JOURNAL, **80**, 148 (1958).

[6] T. C. Bruice and R. Lapinski, *ibid.*, **80**, 2265 (1958).

[7] W. P. Jencks and J. Carriuolo, *ibid.*, **82**, 1778 (1960).

[8] E. R. Garrett, *ibid.*, **79**, 3401, 5206 (1957).

[9] H. Morawetz and P. E. Zimmering, *J. Phys. Chem.*, **58**, 753 (1954).

[10] H. Morawetz and I. Oreskes, *ibid.*, **80**, 2591 (1958).

[11] M. L. Bender, Y. Chow and F. Chloupek, *ibid.*, **80**, 5380 (1958).

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