form[10] in which the *t*-butyl groups can occupy equatorial-like positions. This was shown to be the case (see below), and consequently measurement of the equilibrium between *cis*- and *trans*-I is also a measurement of an equilibrium between the chair and boat forms. From the variation of the equilibrium constant with temperature, the enthalpy and entropy changes accompanying the isomerization were found by methods similar to those employed earlier.[11] The entropy of the cyclohexane system may be presumed to be affected, perhaps seriously, by the presence of the *t*-butyl groups, but the value found for the difference in enthalpy between the boat and chair forms in this case must be quite similar to that of any simple cyclohexane system.

A mixture of the *cis* and *trans* isomers of I was prepared by reducing 2,4-di-*t*-butylphenol using Raney nickel at 180°, then chromic acid oxidation of the mixture of alcohols, and reduction[12] of the resulting ketones.[13] Distillation of the mixture of hydrocarbons through a 4-ft. packed column gave the two isomers: *cis*-I,[13] b.p. 223.3–223.5°, $n^{25}\mathrm{D}$ 1.4531; and *trans*-I,[13] b.p. 229.8–230.0°, $n^{25}\mathrm{D}$ 1.4563. These isomers could be separated cleanly by vapor phase chromatography using a column of glyceryl β-tricyanoethyl ether on firebrick. At 118° the retention times were about 6 and 8 minutes for the *cis* and *trans* compounds, respectively. The analysis showed the *trans* isomer obtained was contaminated with 1.6% of the *cis* while the *cis* contained less than 0.5% *trans*. The *cis* structure was assigned to the isomer of lower enthalpy and physical constants.[14]

Equilibrium between the *cis* and *trans* isomers was established by heating small samples with palladium on carbon catalyst in sealed tubes. The resulting mixtures were analyzed by vapor phase chromatography. The results of the equilibration are given in Table I.

TABLE I

EQUILIBRIUM DATA FOR THE REACTION *cis*-1 ⇄ *trans*-1.[a]

T, °K.	492.6	522.0	555.0	580.0	613.0
% *trans*	2.69	3.61	5.09	6.42	8.23

[a] The % *trans* at any given temperature was obtained from at least eleven analyses on four different samples. Two of these samples approached equilibrium from the *cis* side, and two from the *trans* side. The temperatures are considered accurate to ±1°, and the analysis to ±0.15% *trans*.

A straight line was constructed by the method of least squares which related ln *K* to 1/*T*. From the slope and intercept of the line the values of $\Delta H = +5.9 \pm 0.6$ kcal./mole and $\Delta S = +4.9 \pm 1.0$ e.u. were calculated. This value of ΔH is in reasonable agreement with the predicted values (4.0,[8] 4.75[6] and 5.1[7] kcal./mole).

The experimental value for the entropy clearly indicates that the *trans* isomer is not in the chair form. If it were, the entropy of the reaction would be no more than +1.4 e.u.[15,16]

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[10] Theoretical considerations have indicated that the regular or classical boat form is not the energetically preferred arrangement for the conformation,[6–8] the skewed or "stretched" form is of lower energy. The expression "flexible form" has been used to mean the physically real mixture of these arrangements which is thought to exist. The expression "boat form" is used in this paper to mean the physically existing arrangement other than the chair form, and usually can be taken as synonymous with the expression "flexible form."

[11] (a) N. L. Allinger and J. L. Coke, THIS JOURNAL, **81**, 4080 (1959); (b) N. L. Allinger and J. L. Coke, *ibid.*, **82**, in press (1960).

[12] Huang-Minlon, *ibid.*, **68**, 2487 (1946).

[13] Proper carbon and hydrogen analyses have been obtained for all new compounds.

[14] N. L. Allinger, THIS JOURNAL, **79**, 3443 (1957).

[15] This value is calculated by recognizing that the *trans* isomer in the chair form is a *dl* mixture, while the *cis* is *meso*. It is a *maximum* value, since the axial *t*-butyl group would have its rotational motions restricted much more than would the corresponding equatorial group.

[16] The possibility exists that the *trans* isomer is a mixture which contains an appreciable amount of the chair form with an axial *t*-butyl group. Even if this were the case, the value found for ΔH would still apply to the boat-chair equilibrium as stated.

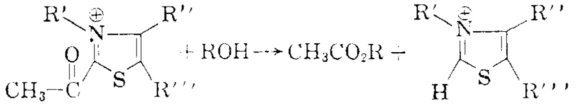
DEPARTMENT OF CHEMISTRY
WAYNE STATE UNIVERSITY
DETROIT 2, MICHIGAN
NORMAN L. ALLINGER
LESLIE A. FREIBERG

RECEIVED JANUARY 30, 1960

ON THE MECHANISM OF THIAMINE ACTION. VI.[1] 2-ACETYLTHIAZOLIUM SALTS AS "ACTIVE ACETATE"

Sir:

Implicit in the mechanism of thiamine action which we have formulated[2] is the requirement that 2-acetylthiamine be able to acetylate phosphoric acid, and thus be yet another form of "active acetate." We wish to report evidence on the kinetic lability of 2-acetylthiazolium salts (I) as support for the idea of their thermodynamic instability as well.



I

Although the weakly basic 2-acetyl-4-methylthiazole,[3,4] from oxidation of the corresponding alcohol,[1] could not be quaternized, its ketal with ethylene glycol, 2-(α-ethylenedioxyethyl)-4-methylthiazole,[3] b.p. 64° (0.15 mm.) $n^{25}\mathrm{D}$ 1.5170, was reactive toward alkyl halides. The quaternary benzyl bromide salt,[3] m.p. 166–167°, was recovered in 80% yield from two days standing in 47% HBr at room temperature, but the remainder was quantitatively accounted for as 3-benzyl-4-methylthiazolium bromide. It is thus apparent that the intermediate 2-acetylthiazolium salt from this ketal hydrolysis is deacetylated by the medium, although the deacetylation of such a cation is unlikely to be acid catalyzed.

A much more striking indication of the instability of these acetyl compounds is found in the studies on 3,4-dimethyl-2-(α-hydroxyethyl)-thiazolium nitrate,[3] m.p. 133–134°, prepared from the iodide[1] by ion exchange. Oxidation of this compound with *t*-butyl hypochlorite in nitromethane, and ether precipitation of the thiazolium salts, afforded a mixture whose infrared absorption at 5.85 μ and ultraviolet absorption (in dimethoxyethane)

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[1] For part V, see R. Breslow and E. McNelis, *ibid.*, **81**, 3080 (1959).

[2] R. Breslow, *ibid.*, **80**, 3719 (1958).

[3] Satisfactory C, H and N analyses were obtained for these compounds.

[4] J. Metzger and B. Koether, *Bull soc. chim. France*, 702 (1953).

at 253 and 294 mμ were consistent with the presence of the expected 2-acetylthiazolium salt. The band near 300 mμ, which is characteristic of the 2-acetyl substituted thiazole chromophore, was absent when the spectra were run in water or methanol. Furthermore, solution of the mixture for ten minutes in methanol at room temperature, then ether precipitation, led to a 50% decrease in the intensity of the carbonyl band at 5.85 μ, accompanied by the appearance of a new band at 10.7 μ; repeated methanol treatment led to further decrease in the carbonyl band and increase in the 10.7 μ absorption. Since this latter is the C–H bending vibration characteristic of thiazolium salts unsubstituted at C-2[2], it is apparent that the process being observed is a deacylation at C-2.

The leaving group in the deacylation reaction is the same thiazolium zwitterion which has been detected previously,[2] but the lability of the 2-acetylthiazolium salts is much greater than would be expected solely from the stability of this thiazolium zwitterion, and it seems likely that dipole-dipole repulsion in the ketone is also an important factor. At any rate, these results furnish additional support for the mechanism of thiamine action already proposed.

DEPARTMENT OF CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK, NEW YORK
RONALD BRESLOW
EDWARD MCNELIS

RECEIVED MARCH 17, 1960

VERIFICATION OF THE ONSAGER LIMITING LAW FOR TRACE-ION DIFFUSION IN ELECTROLYTE SOLUTIONS

Sir:

In 1945, Onsager[1] formulated a theoretical expression for the concentration-dependence of trace-ion diffusion and his equations later were translated into a more practical form and also adapted to the self-diffusion case by Gosting and Harned[2] in 1951. The resulting equation for 1:1 electrolytes at 25° is of the form

$$D_{\mathrm{j}} = D_{\mathrm{j}}^{\circ}\ [1 - 0.7816(1 - \sqrt{d(w)_{\mathrm{j}}})\sqrt{c}] \qquad (1)$$

$d(w_{\mathrm{j}})$ being a function of the mobilities and valencies of the ions. This is the only limiting equation stemming from the Debye–Hückel theory of interionic attraction that has not been tested experimentally. The usual experimental diffusion methods are inadequate; the diaphragm cell gives inaccurate data in the dilute concentrations due to adsorption effects and the normal open-ended capillary method has, at best, a precision of *ca.* ±1%.

However, the continual monitoring capillary method, developed by Mills and Godbole,[3,4] can provide data with precision better than ±0.2% and should therefore be capable of testing the law. We wish to report self-diffusion coefficients of Na^+ ion in dilute sodium chloride solutions as determined with this method. Table I shows the results obtained to date, of an average precision of ± 0.18%, together with values calculated from the limiting law.

TABLE I

c, mole/l.	D(obs.) cm.²/sec.	D(calcd.) cm.²/sec.
0.000225	1.335	1.330
.00076	1.332	1.326
.00102	1.327	1.325
.00500	1.319	1.315
.0101	1.312	1.307
.0252	1.297	1.291
.0286	1.298	1.288
.0495	1.294	1.274
.0575	1.289	1.269
.097	1.280	1.250

Extrapolation of the last four points gives a D° of 1.337 compared with the Nernst limiting value of 1.334.

The results also are illustrated in Fig. 1. It will be observed that for concentrations <0.002*M*, the limiting equation appears to be valid. Further, by replacing the factor $\sqrt{c}$ in equation (1) by $\sqrt{c}/(1 + \kappa a)$, the experimental points can be described to *ca.* 0.04*M*, using an "*a*" value of 4Å.

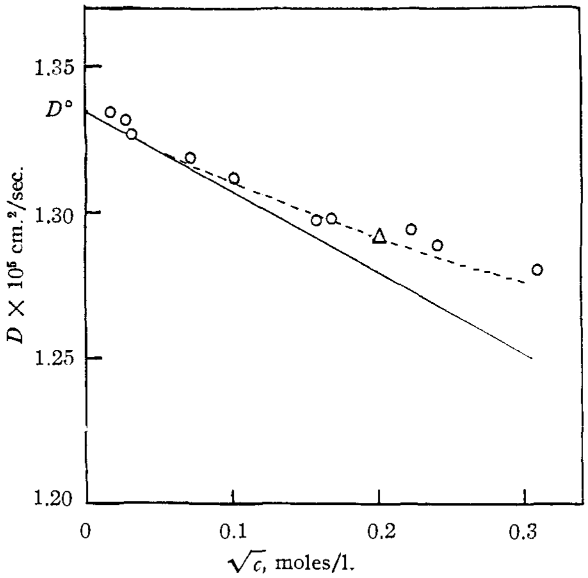

Fig. 1.—Self-diffusion coefficients of Na^+ in aqueous sodium chloride at 25°: O, this work; Δ, Mills and Adamson; ———, Onsager limiting slope; – – – –, ion size extension (å = 4).

A feature of the experimental method that is not entirely satisfactory and needs further investigation, is the question of the correct flow rate to be maintained across the mouth of the capillary. We have attempted to overcome this difficulty by calibrating the apparatus for flow conditions against the Na^+ self-diffusion data of Mills and Adamson.[5] Agreement for a specified flow is obtained with their data at concentrations of 0.04*M* and 1.44*M*. However, this calibration procedure is an indirect method since the cell has in turn to be calibrated against optical data and, further, the average precision of Mills and Adamson's data is only of the order of ±0.4%.

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(1) L. Onsager, *Ann. N. Y. Acad. Sci.*, **46**, 241 (1945).

(2) L. J. Gosting and H. S. Harned, THIS JOURNAL, **73**, 159 (1951).

(3) R. Mills and E. W. Godbole, *Aust. J. Chem.*, **11**, 1 (1958).

(4) R. Mills and E. W. Godbole, *ibid.*, **12**, 102 (1959).

(5) R. Mills and A. W. Adamson, THIS JOURNAL, **77**, 3454 (1955).