third to fourth days, etc. The seventh column in the table contains the mean value of these results.

Theoretical Considerations

The theoretical values[5] of the diffusion coefficient were computed by means of equations (1), (2), (3) and (4) of Harned and Nuttall.[4] The data required for this computation are compiled at the bottom of the Table I. The values of the dielectric constant, D, and the viscosity, η_0, were taken from Tables (5-1-3) and (5-3-1) of Harned and Owen.[6] The equivalent limiting conductances are those derived recently by Professor B. B. Owen from a comprehensive investigation of the conductances of the alkali halides. The activity coefficient function was computed from the activity coefficients of Harned and Cook.[7] The parameters A' and B were recalculated using a value of the limiting slope of the Debye and Hückel theory, $S_{(f)}$, computed by the universal constants of Birge.[8] The required density data were obtained from the computation of Scott.[9]

With these values, the theoretical equations for the diffusion coefficient of potassium chloride, **D**, at 4° become

$$\mathbf{D} = 4.609 \times 10^{13} \left(\frac{\overline{M}}{c}\right)\left[1 + c\,\frac{\partial \ln y_{\pm}}{\partial c}\right] \qquad (2)$$

$$\frac{\overline{M}}{c} \times 10^{20} = 24.630 - 0.00049\,\frac{\sqrt{c}}{(1 + 1.170\sqrt{c})} + 10.34c\,\phi\,(1.170\sqrt{c}) \qquad (3)$$

$$\left[1 + c\,\frac{\partial \ln y_{\pm}}{\partial c}\right] = 1 - \frac{0.5657\sqrt{c}}{(1 + 1.170\sqrt{c})^2} + 0.032\,c - c\psi(d) \qquad (4)$$

$$c\psi(d) = \frac{0.0125c - 0.0047c^{3/2}}{1.0000 + 0.0125c - 0.0031c^{3/2}} \qquad (5)$$

Comparison of the theoretical values, given in the last column of Table I, with the observed values shows agreement within the estimated experimental error up to the highest concentration. This behavior is identical with that found at 25°,[2,3,4] and is not very significant since one would not expect the theory to be valid at the higher concentrations. Dr. Louis J. Gosting has made one accurate determination of the diffusion coefficient of potassium chloride at 1° by the Gouy interference method[10,11,12] which he has kindly put at our disposal before publication. He obtained 0.954×10^{-5} at 0.300 molar for this quantity at 1°. After estimation of the temperature coefficient from the theoretical equations, we obtain 1.053×10^{-5} at 4°, a result which is about 1% higher than that obtained by the conductance method.

Summary

1. The diffusion coefficient of potassium chloride in water has been determined at 4° at concentrations between 0.01 and 0.6 molar.

2. Agreement with the theory of Onsager and Fuoss was found throughout the above range of concentrations. This result is in accord with previous observations at 25°.

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[5] Onsager and Fuoss, *J. Phys. Chem.*, **37**, 2689 (1932).

[6] Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corporation, New York, N. Y., 1943.

[7] Harned and Cook, This Journal, **59**, 1290 (1937) [see also ref. (6), p. 558].

[8] Birge, *Rev. Mod. Phys.*, **13**, 233 (1941).

[9] Scott, *J. Phys. Chem.*, **35**, 2315 (1931).

[10] Kegeles and Gosting, This Journal, **69**, 2516 (1947).

[11] Gosting and Morris, *ibid.*, **71**, 1998 (1949).

[12] Gosting, Hanson, Kegeles and Morris, *Rev. Sci. Instr.*, **20**, 209 (1949).

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[Contribution from Carson-Newman College]

Some Quaternary Salts of Hexamethylenetetramine[1]

By Carl T. Bahner, Madge D. Pickens, Donald Pickens and William K. Easley

The biological results obtained by Shear and associates[2] at the National Cancer Institute using quaternary salts derived from pyridine and its homologs and benzologs have led us to undertake the preparation of several series of similar quaternary salts containing other heterocyclic rings.[3] In a previous article[4] 23 salts containing the thiazole ring were reported, none of which has as yet given positive results in cancer chemotherapy screening tests. On the other hand, very dilute aqueous solutions of a number of members of a series of hexamethylenetetraminium salts have been found to have an effect of the same order of magnitude as nitrogen mustard in inhibiting the respiration of rabbit bone marrow cells in serum, in preliminary tests by Dr. C. E. Carter and associates, of Oak Ridge National Laboratories, and have been submitted to Dr. M. J. Shear and associates, of the National Cancer Institute, for screening tests against sarcomas in mice, results of which are to be reported elsewhere.

In 1915 Jacobs and Heidelberger[5] prepared an extensive series of quaternary salts of hexamethylenetetramine for other purposes. Several of their preparations have been repeated and in addition the salts listed in Table I have been prepared.

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[1] Presented in part at the Atlantic City meeting of the American Chemical Society, September, 1949.

[2] Shear, *et al.*, in "Approaches to Cancer Chemotherapy," American Association for the Advancement of Science, F. R. Moulton, Editor, Washington, D. C., 1947, p. 236 ff.; Hartwell and Kornberg, This Journal, **68**, 1131 (1946).

[3] Bahner and Pickens, *J. Tenn. Acad. Sci.*, **23**, 104 (1948).

[4] Bahner, Pickens and Bales, This Journal, **70**, 1652 (1948).

[5] Jacobs and Heidelberger, *J. Biol. Chem.*, **21**, 455 (1915).

TABLE I

HEXAMETHYLENETETRAMINE DERIVATIVES

Salt from hexamethylenetetramine and Bromide	Empirical formula	M. p., °C.	Ionic halogen, % Calcd.	Ionic halogen, % Found[a]
p-Fluorophenacyl	$C_{14}H_{18}BrFN_4O$	126–128 dec.	22.24	21.93
p-Chlorophenacyl	$C_{14}H_{18}BrClN_4O$	153 dec.	21.33	21.32
p-Bromophenacyl	$C_{14}H_{18}Br_2N_4O$	153–154 dec	19.11	18.86
p-Iodophenacyl	$C_{14}H_{18}BrIN_4O$	172 dec.	17.19	17.09
p-Iodophenacyl oxime	$C_{14}H_{19}BrIN_5O$	128 dec.	16.64	16.41
2,4-Dichlorophenacyl	$C_{14}H_{17}BrCl_2N_4O$	167–168 dec.	19.58	19.28
p-Phenylphenacyl[b]	$C_{20}H_{23}BrN_4O$	153–154 dec.	19.24	19.01
β-Naphthacyl[c]	$C_{18}H_{21}BrN_4O$	152 dec.	20.53	20.43
Iodide				
p-Chlorophenacyl	$C_{14}H_{18}ClIN_4O$	172–173 dec.	30.17	30.06
p-Bromophenacyl	$C_{14}H_{18}BrIN_4O$	170–171 dec.	27.29	27.31
p-Iodophenacyl	$C_{14}H_{18}I_2N_4O$	180–181 dec.	24.78	24.60
5,6,7,8-Tetrahydro-β-naphthacyl	$C_{18}H_{25}ION_4$	165–166 dec.	28.83	28.53
p-Phenylphenacyl	$C_{20}H_{23}ION_4$	176–177 dec.	27.45	27.60

[a] Average of two Volhard analyses in each case. [b] Prepared by Mr. Richard D. Allen. [c] *Cf.* Immediata and Day, *J. Org. Chem.*, **5**, 512 (1941).

In nearly every case the white quaternary salt precipitated within a short time when chloroform solutions of hexamethylenetetramine and the organic halide were mixed at room temperature and was obtained in 80–98% yield in a satisfactory degree of purity upon washing with chloroform and drying. Recrystallization was avoided because of the tendency of these products toward decomposition in solution. The volume of solvent used for the reaction was not found to be a critical factor, but was usually slightly more than the minimum amount required to dissolve the reactants at room temperature. Since 5,6,7,8-tetrahydro - β - naphthacylhexamethylenetetraminium iodide was soluble in chloroform this product was precipitated from the reaction mixture two hours after mixing by the addition of acetone in excess and the white crystals were washed with acetone. In the preparation of *p*-chlorophenacylhexamethylenetetraminium bromide one run was made in which the reaction mixture was allowed to stand overnight before filtering. The product, m. p. 145° dec., was found to contain 24.15% bromide in contrast with 21.33% calculated for $C_{14}H_{18}BrClN_4O$. However, when the preparation was repeated and the product filtered off at the end of one hour, the white crystals obtained in over 90% yield, m. p. 153° dec., contained 21.33% bromine and appeared to be pure. After this observation it was decided to sacrifice yields in favor of purity and to filter off the product at the end of one-half hour instead of waiting for the reaction to go to completion.

The hexamethylenetetraminium salts containing large hydrocarbon radicals were found to be only sparingly soluble in cold water and the water solutions were not stable over long periods of time, but the dry compounds have been kept several months at room temperature before signs of decomposition were noted. Decomposition temperatures observed by heating samples slowly in conventional melting point tubes were relatively sharp and are indicated in the accompanying table, but it is well known that decomposition temperatures of such compounds are somewhat variable.

The *p*-iodophenacyl bromide oxime was prepared by a procedure analogous to that used by Korten and Seboll[6] to prepare *syn*-phenacyl bromide oxime.

Additional compounds of the series are being prepared and also compounds suspected to be among the intermediate and final products of hydrolysis of the salts.

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Summary

Several new phenacyl and naphthacyl halide salts of hexamethylenetetramine have been prepared. Compounds of this series appear to be active in inhibiting cell respiration.

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[6] Korten and Seboll, *Ber.*, **34**, 1907 (1901).