Organic Reactions Occurring in or on Micelles. III. Reaction of Methyl Bromide with Cyanide Ion[1,2]

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Salt effects have been measured at 20.00° on the distribution constant h of methyl bromide between gas phase and aqueous solution, and on the second-order rate constant, k_2, for its reaction with cyanide ion. NaCN and NaBr produce small, salting-out effects on h and small increases of k_2. Salt effects due to the anionic detergent, sodium laurylsulfate, are large and in the opposite direction; they are consistent with the theory that methyl bromide is distributed between bulk phase and micelle phase according to the law of mass action, and that the micelle phase is unreactive. Salt effects due to the cationic detergent, lauryltrimethylammonium bromide, indicate that a substantial fraction of methyl bromide exists in the micelle phase, and that k_2 for this fraction is 30–50 times larger than k_2 for methyl bromide in the bulk. Distribution constants have been measured also for acetonitrile between gas phase and aqueous solution at 20.00°.

Aqueous solutions of detergent salts are useful solvent media for organic reactions because the formation of a micelle phase provides a convenient mechanism for controlling reaction rates and products.[2-6] The electrical charge of the micelle-forming detergent ions is screened only partially by counterions in the double layer. For example, the electrical potential of the micelles formed from a cationic detergent will be positive with respect to that of the bulk phase. As a result, if an organic substrate is solubilized by a detergent, a reaction in which that substrate is attacked by an anion can be facilitated by the use of a cationic detergent and retarded by the use of an anionic detergent.

We now report a quantitative study of the effect of sodium laurylsulfate (NaLS) and lauryltrimethylammonium bromide (DetBr) on the reaction of methyl bromide with cyanide ion in aqueous solution (eq. 1). Methyl

$$CH_3Br + CN^- \xrightarrow{k_2} Br^- + CH_3CN \qquad (1)$$
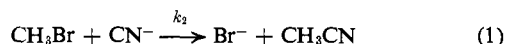
bromide is quite volatile in aqueous solution, and its thermodynamic activity and rate of reaction can be determined manometrically with high accuracy.[7,8]

(1) This work was supported by the Office of Naval Research. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(2) Previous papers in this series: (a) E. F. J. Duynstee and E. Grunwald, *J. Am. Chem. Soc.*, 81, 4540 (1959); (b) *ibid.*, 81, 4542 (1959).

(3) K. G. van Senden and C. Koningsberger, *Tetrahedron Letters*, No. 1, 7 (1960).

(4) M. B. Lowe and J. N. Phillips, *Nature*, 190, 262 (1961).

(5) J. L. Kurz, *J. Phys. Chem.*, 66, 2239 (1962).

(6) (a) M. T. A. Behme and E. H. Cordes, *J. Am. Chem. Soc.*, 87, 260 (1965); (b) M. T. A. Behme, J. G. Fullington, R. Noel, and E. H. Cordes, *ibid.*, 87, 266 (1965).

(7) R. W. Taft, E. L. Purlee, and P. Riesz, *ibid.*, 77, 899 (1955).

(8) G. A. Clarke, T. R. Williams, and R. W. Taft, *ibid.*, 84, 2292 (1962), and references cited therein.

In our experiments, a known quantity of methyl bromide was added to a known quantity of outgassed aqueous solution in an apparatus of known volume, and the distribution constant of methyl bromide between gas phase and liquid phase was calculated from the rapid pressure drop that started immediately when the system was stirred.[7] The rate of reaction of methyl bromide was slow compared to its rate of distribution between gas and liquid phase and was measured by means of the further pressure drop that takes place in the stirred system over a prolonged period of time. We also report some salt-effect studies involving sodium bromide and sodium cyanide, for comparison with those on the detergent salts.

While sodium bromide and sodium cyanide cause relatively small increases in the thermodynamic activity of methyl bromide in aqueous solution, the detergent salts cause rather large decreases in the activity. The effects of the detergent salts are quantitatively consistent with the theory that the reduced activity is the result of a distribution of methyl bromide between an aqueous bulk phase and a micelle phase.

Salt effects on the second-order rate constant, k_2, for reaction 1 are as follows. Sodium bromide and sodium cyanide cause small increases, sodium laurylsulfate causes a large decrease, and lauryltrimethylammonium bromide causes a very large increase. The effects of NaBr and NaCN on k_2 are in the same direction as those on the activity of methyl bromide, but they are smaller; $\delta \log k_2/\delta \log$ (activity) ≈ 0.4. The effect of sodium laurylsulfate is quantitatively consistent with the theory that the fraction of methyl bromide that exists in the micelle phase is unreactive. The effect of lauryltrimethylammonium bromide is consistent with the theory that the fraction of methyl bromide that exists in the micelle phase is about 40 times as reactive as the fraction that exists in the bulk.

Results

Distribution Constants. The equilibrium constant, h, for distribution of methyl bromide between gas phase and liquid phase is defined in eq. 2, where p is the partial pressure of CH_3Br in the gas phase (in atm.) and c is its molar concentration in the liquid phase. Ex-

$$h = c/p \text{ [mole/l. atm.]} \qquad (2)$$

perimental results are summarized in Table I. The accuracy of the h values is estimated conservatively at $\pm 1\%$. It is clear from experiments 1 and 2, 7 and 8, and 9 to 11 that Henry's law is obeyed quantitatively even in the presence of a detergent salt.

Table I also lists values of the activity coefficient, f, of methyl bromide in the salt solutions, where $f =$

Table I. Distribution Constants, h, of Methyl Bromide between Gas Phase and Aqueous Salt Solutions at 20.00°

No.	CH_3Br partial pressure, atm.	Salt, mole/l.	h, mole/l. atm.	$f = h_0/h$
1	0.0932	...	0.185$_9$	1.00$_0$
2	0.1261	...	0.186$_6$	1.00$_0$
3	0.1541	NaCN, 0.025	0.186$_2$	1.00$_0$
4	0.1546	NaCN, 0.250	0.170$_6$	1.09$_1$
5	0.1709	NaCN, 0.957	0.154$_1$	1.20$_8$
6	0.1033	NaCN, 0.250; NaBr, 0.297	0.157$_7$	1.18$_1$
7	0.2914	NaLS,^{a} 0.098	0.228$_3$	0.81$_6$
8	0.4329	NaLS, 0.098	0.228$_8$	0.81$_4$
9	0.0416	NaLS, 0.304	0.321$_5$	0.57$_9$
10	0.1154	NaLS, 0.304	0.319$_5$	0.58$_3$
11	0.2203	NaLS, 0.304	0.321$_5$	0.57$_9$
12	0.1659	NaCN, 0.194; NaLS, 0.303	0.300$_3$	0.62$_0$
13	0.1738	NaCN, 0.099; DetBr,^{a} 0.302	0.348$_4$	0.53$_4$

^{a} NaLS = sodium laurylsulfate, $NaO_3SOC_{12}H_{25}$; DetBr = lauryltrimethylammonium bromide, $C_{12}H_{25}N(CH_3)_3Br$.

h_0/h where h_0 is the distribution constant in pure water and h is that in the salt solution. Thus the reference state for f is the highly dilute solution of methyl bromide in salt-free water.[9] Evidently, NaCN and NaBr cause some salting out ($f > 1$). If we assume the validity[10] of Sechenoff's equation (3) (our data are insufficient to test this assumption), then "best values" of the parameter S_f are 0.15 for NaCN and 0.12 for NaBr, up to about 0.3 M concentrations of these salts.

$$\log f = S_f c_{salt} \qquad (3)$$

In preparing Table II, we have used these values of S_f in conjunction with eq. 3 for purposes of interpolation.

Table II. Distribution of Methyl Bromide between Micelle Phase and Aqueous Bulk Phase at 20.00°

Detergent salt, mole/l.	h/h_B	$c_{micelle}$	K
$NaO_3SOC_{12}H_{25}$, 0.098	1.227^a	0.092^b	2.47
$NaO_3SOC_{12}H_{25}$, 0.304	1.723^a	0.298^b	2.43
$NaO_3SOC_{12}H_{25}$, 0.303 + NaCN, 0.194	1.727^c	0.297^b	2.45
		Av.	2.45
$C_{12}H_{25}N(CH_3)_3Br$, 0.302 + NaCN, 0.099	1.937^d	0.302^e	3.10

^{a} h_B = 0.1862. ^{b} Critical micelle concentration = 0.006 M: P. Mukerjée and K. J. Mysels, *J. Am. Chem. Soc.*, **77**, 2937 (1955). ^{c} h_B = 0.1739, which is the value of h for 0.194 M NaCN. ^{d} h_B = 0.1799, which is the value of h for 0.099 M NaCN. ^{e} Critical micelle concentration < 0.001 M: E. L. Colichman, *J. Am. Chem. Soc.*, **72**, 4036 (1950).

In interpreting the distribution constants for solutions containing a detergent salt, we shall assume that the formal liquid phase concentration, c, of methyl bromide can be separated into two additive terms, as in eq. 4, where c_B denotes the actual molar concentration

(9) C. A. Clarke and R. W. Taft, *J. Am. Chem. Soc.*, **84**, 2295 (1962).
(10) F. A. Long and W. F. McDevit, *Chem. Rev.*, **51**, 119 (1952).

$$c = c_B + c_M \qquad (4)$$

of methyl bromide in the bulk phase, and c_M denotes the moles of methyl bromide solubilized in the micelle phase per liter of macroscopic solution. We shall assume, further, that c_M is related to c_B by an appropriate distribution constant according to the law of mass action (eq. 5). Equation 5 applies to moderately low

$$\frac{c_M}{c_B} = K c_{micelle} \qquad (5)$$

detergent concentrations so that the volume fraction of the micelle phase is $<< 1$. Under these conditions, the ratio c_M/c_B is proportional to the volume fraction of the micelle phase and hence to $c_{micelle}$, the formal concentration of detergent salt that exists in the form of micelles. The latter is given by eq. 6, where $c_{det. salt}$ is the total concentration and c_{CMC} is the critical micelle concentration for the given solution. Since

$$c_{micelle} = c_{det. salt} - c_{CMC} \qquad (6)$$

$c = hp$ (eq. 2), eq. 4–6 can be rewritten so that the variables are distribution constants. The result is eq. 7. In this equation, h is the distribution constant

$$h/h_B = 1 + K(c_{det. salt} - c_{CMC}) \qquad (7)$$

for the solution that contains the detergent salt, and h_B (B for bulk phase) is the distribution constant for an otherwise identical solution but without the detergent salt.

Equation 7 can be tested by our data on solutions containing sodium laurylsulfate and gives good fit, as shown in Table II. It is evident from the data that eq. 7 is not merely a limiting law that becomes exact at low substrate concentrations; the fit is better than 1% even though the formula weight ratio of methyl bromide to laurylsulfate ($c_M/c_{micelle}$) in the micelle phase is as high as 1:5.

Rate Constants. Second-order rate constants, k_2, for reaction 1 are summarized in Table III. The accuracy of these results is estimated conservatively at $\pm 2\%$. It is seen that NaCN and NaBr produce small positive salt effects. If we assume that these effects can be represented[9] by eq. 8 (our data are insufficient to test this assumption) then "best values" of the parameter S_k are 0.06 for either salt. In preparing

$$\log k = \log k_0 + S_k c_{salt} \qquad (8)$$

Table IV we have used these values in conjunction with eq. 8 for purposes of interpolation. The "best values" of S_k are about four-tenths as large as the corresponding values of S_f (see eq. 3).

In interpreting the data obtained for solutions containing detergent salts, we shall assume that the formal rate constant, k_2, can be separated into two additive terms, one for reaction in the bulk phase and the other for reaction in the micelle phase (eq. 9). Upon intro-

$$k_2 = (k_B c_B + k_M c_M)/c \qquad (9)$$

Table III. Second-Order Rate Constants for Reaction of CH_3Br with NaCN in Aqueous Solutions of Detergent Salts at 20.00°

NaCN, mole/l.	Salt, mole/l.	$10^4 k_2$, l. mole^{-1} sec.$^{-1}$	k_2/k_2^0
0.000	...	(6.30)^a	1.00$_0$
0.025	...	6.32	1.00$_3$
0.250	...	6.60	1.04$_7$
0.957	...	6.74	1.07$_0$
0.250	NaBr, 0.297	6.68	1.06$_0$
0.194	NaLS, 0.303	3.78	0.60$_0$
0.099	Det Br, 0.302	153.5	24.4
0.189	Det Br, 0.302	87.5	13.9

^{a} Extrapolated.

ducing eq. 4–7, eq. 9 can be transformed into eq. 10

$$k_2 = \frac{k_B}{1 + Kc_{\text{micelle}}} + \frac{k_M Kc_{\text{micelle}}}{1 + Kc_{\text{micelle}}} \quad (10)$$

where k_2 is the rate constant for the solution containing the detergent salt, k_B is the rate constant for an otherwise identical solution but without the detergent salt, and k_M is the (microscopic) rate constant for reaction in the micelle phase. We are assuming in eq. 10 that the rate of distribution across the phase boundary is very fast compared to the rate of the chemical processes.

reaction mixtures indicates that the major portion of the product is acetonitrile.[14]

Experimental Section

Materials. The water used in preparing the solutions was redistilled from alkaline permanganate. Sodium bromide and sodium cyanide were Baker Analyzed reagents. The concentration of the sodium cyanide solutions was determined by titration with silver nitrate. Methyl bromide (99.5% pure) was obtained from the Matheson Co., Inc. The acetonitrile (Fisher reagent grade) was distilled over phosphorus pentoxide.

Sodium laurylsulfate was prepared from Eastman Kodak Co. White Label *n*-lauryl alcohol according to procedure of Dreger.[15] The product was recrystallized twice from 95% ethanol and dried under vacuum. Lauryltrimethylammonium bromide was prepared from *n*-lauryl bromide (Eastman Kodak Co. White Label) and trimethylamine (Eastman Kodak Co. White Label).[16] The product was recrystallized thrice from acetone and finally dried under vacuum.

Measurements and Calculations. All experiments were carried out in a water thermostat at 20.00 ± 0.01°. Distribution constants and rate constants were measured in a single apparatus by a method that was developed by Levy, *et al.*,[17] and has since been improved by others.[7,8] Our apparatus was almost

Table IV. Analysis of Rate Constants for Reaction 1 on the Basis of Eq. 10^a

Detergent salt,^{b} M	NaCN, M	c_B/c	Rate constant, l./mole sec.		
			$10^4 k_2$	$10^4 k_B$	$10^4 k_M$
NaLS, 0.303	0.194	0.579	3.78 ± 0.04	6.47 ± 0.06	0.07 ± 0.14
Det Br, 0.302	0.099	0.517	154 ± 8	6.39 ± 0.06	311 ± 16
	0.189	0.517	88 ± 4	6.47 ± 0.06	174 ± 8

^{a} Data for aqueous solutions of detergent salts at 20.00°. ^{b} NaLS = sodium laurylsulfate; DetBr = lauryltrimethylammonium bromide.

An analysis of the kinetic data on the basis of eq. 10 is presented in Table IV. When the solution contains sodium laurylsulfate, k_M is indistinguishable from zero. When the solution contains lauryltrimethylammonium bromide, k_M is appreciably greater than k_B. The decreasing trend of k_M with increasing NaCN concentration is real, but we did not try to identify the physical mechanism that is causing it.

The usual product isolated from the reaction between a methyl halide and an alkali cyanide in homogeneous solution is acetonitrile.[11] However, cyanide ion is an ambient anion,[12] and under certain conditions the product is CH_3NC rather than CH_3CN. For example, the use of AgCN rather than NaCN leads to the formation of some isocyanide.[13] It has been pointed out[12] that when reaction between an ambient anion and an organic substrate molecule takes place at an interphase, the product can be quite different from that obtained in homogeneous solution. However, in the present case, the vapor phase chromatograph of the

identical with Purlee's,[7] except that a powerful Mag-Mix magnetic stirrer was used instead of a reciprocating shaker. The Mag-Mix stirrer was mounted directly under the thermostat, approximately 1–2 in. below the reaction vessel. Vapor pressures were measured to ±0.005 cm. on a mercury manometer constructed of precision glass tubing. A Gaertner cathetometer was used to take readings.

Methyl bromide vapor at a known temperature above 20° was introduced into the apparatus containing a known volume of unstirred solvent or salt solution. In the absence of stirring, the pressure changes only slowly because the rate of solution of gaseous methyl bromide is quite slow. Pressure readings were taken on the unstirred system over several minutes, until enough data had been obtained to allow accurate extrapolation to zero time. Stirring was then commenced, and the pressure dropped rapidly to a new

(11) B. W. Marshall and E. A. Moelwyn-Hughes, *J. Chem. Soc.*, 2640 (1959).
(12) For example, N. Kornblum and A. P. Lurie, *J. Am. Chem. Soc.*, 81, 2705 (1959).
(13) H. L. Jackson and B. C. McKusick, *Org. Syn.*, 35, 62 (1955).

(14) Unfortunately, this work had to be discontinued before the presence or absence of methyl isocyanide could be determined with absolute certainty.
(15) E. E. Dreger, G. I. Keim, G. D. Miles, L. Shedlovsky, and J. Ross, *Ind. Eng. Chem.*, 36, 610 (1944).
(16) A. B. Scott and H. V. Tartar, *J. Am. Chem. Soc.*, 65, 692 (1943).
(17) J. B. Levy, R. W. Taft, D. Aaron, and L. P. Hammett, *ibid.*, 73, 3972 (1951).

value that was characteristic of the saturated solution. If the solution did not contain the reactant, sodium cyanide, the distribution constant was calculated[7] from the pressure at zero time (extrapolated value) and the equilibrium pressure (final reading). When the solution contained sodium cyanide the pressure would continue to drop slowly after stirring owing to chemical reaction. The equilibrium pressure was then determined as in ref. 8. It was found that reaction 1 is accurately second order, first order each in methyl bromide and in cyanide ion, regardless of the nature and concentration of added salt. The parameter, k_2, in eq. 11 or 12 remained constant throughout the course of any single kinetic run, up to 98% completion of the reaction.

$$\ln\left[\frac{P_0 - P_\infty}{P - P_\infty}\right] + \ln\left[1 - \frac{(P_0 - P)\mu\mu_{RCN}}{[CN^-]_0(\mu_{RCN} - \mu)}\right] = k_2 t\left[\frac{[CN^-]_0 h}{\mu} - [CH_3Br]_0\right] \quad (11)$$

if CN^- is in excess.

$$\ln\left[\frac{P_0 - P_\infty}{P - P_\infty}\right] + \ln\left[1 - \frac{(P_0 - P)\mu_{RCN}h}{[CH_3Br]_0(\mu_{RCN} - \mu)}\right] = k_2 t [CH_3Br]_\infty \quad (12)$$

if CH_3Br is in excess. In these equations, P is the pressure reading on the manometer at time t, $\mu \equiv (r/(RT) + h)$, $\mu_{RCN} \equiv (r/(RT) + h_{RCN})$, r = volume of gas phase divided by the volume of liquid phase, h = distribution constant of methyl bromide, h_{RCN} = distribution constant of acetonitrile, and formulas in brackets denote the respective molar concentrations at described times.

Equations 11 and 12 were derived by the general procedure of Clarke, Williams, and Taft[8] for a second-order reaction. The methyl bromide (reactant) and acetonitrile (product) are considered to be the volatile species. The formation of methyl isocyanide has been neglected. Distribution constants, h_{RCN} and h_{RNC}, are listed in Table V. The values of h_{RCN} were measured in fairly concentrated solution but could be readily extrapolated to infinite dilution.

On comparing the data in Table V with those in Table I, it is seen that methyl bromide is far more volatile than any of the products. Values of P_∞ were therefore calculated from measured values of P_0, the vapor pressure of the solvent, and from the known ratio h/h_{RCN} of the distribution constants.

Table V. Distribution Constants for Reaction Products between Gas Phase and Aqueous Solution at 20.00°

Reaction product, mole/l.	ϕ^a	h_{RCN} or h_{RNC}, moles/l. atm.	h_{RCN}, calcd.[b]
CH_3CN, 0.000	...	...	56.2
1.318	0.0645	58.1	57.8
2.728	0.1250	62.5	62.8
5.957	0.2377	84.0	84.0
CH_3NC, 1.8[c]	...	9[d]	

[a] ϕ = volume fraction of CH_3CN in aqueous solution. [b] From the equation $\log h_{RCN} = 1.750 + 3.10\ \phi^2$. [c] Approximate solubility in water: F. K. Beilstein, "Handbuch der organischen chemie," Vol. IV, p. 56. [d] Vapor pressure of pure liquid divided by the solubility in water.

Some Observations on Aqueous Solutions of Detergent Salts. It is remarkable that when one adds 4.9 g. of sodium cyanide to a solution containing 20 g. of cetyltrimethylammonium bromide and 1.3 g. of *n*-butyl bromide in 180 g. of water at room temperature, a gel is formed. An aqueous solution containing approximately the same molal concentration of cetyltrimethylammonium bromide (0.294 *m*) and sodium cyanide (0.523 *m*) has a viscosity of about 0.15 poise at 25°, more than 15 times that of water.

Analysis of Products. An authentic sample of methyl isocyanide was prepared from methyl iodide and silver cyanide.[13] The gas phase chromatographic analyses were accomplished with a 15 ft. $\times$ 0.25 in. column of 5% Carbowax-20M on Chromport at 62°, and with a helium flow rate of 140 cc./min. While mixtures containing only acetonitrile and methyl isocyanide were separated into two, well-resolved peaks, the dilute aqueous solutions of acetonitrile and methyl isocyanide gave only the acetonitrile and water peaks. Several other columns behaved similarly. This problem is being investigated further by L. J. Winters.