Journal of the Pharmaceutical Society of Korea
18, 183-189 (1974)

Studies on the Distribution Coefficient of the Primary, Secondary, Tertiary Amine and Quaternary Ammonium-methylorange Salts.

Bak-Kwang Kim

(Received May 8, 1974)

Abstract—Distribution coefficients between nitrobenzene solution and deionized water, show a straight line when the number of alkyl radicals against the logarithm of distribution coefficient of the salts was plotted. After extracting salts of the indicator and the cationic surfactants with organic solvents, and employing the colorimetric method was used. A calculation method of distribution coefficients of the salts in the organic solvent has been suggested and it could be used for the extraction equilibrium of the primary amine, $CH_3(CH_2)_nNH_3^+$, secondary amine, $CH_3(CH_2)_nNH_2(CH_3)^+$, tertiary amine, $CH_3(CH_2)_nNH(CH_3)_2^+$ and quaternary ammonium, $CH_3(CH_2)_nN(CH_3)_3^+-MO^-$ salts, (n=3, 5, 7, 11).

Recently, studies for the interaction of surfactants and indicators[1~5] have been practised widely. These studies were made for the purpose of developing the mechanism of salts, such as in the extraction procedure[6~9].

Nitrobenzene solution (N.B. solution) of salts was added to deionized water saturated with N.B. organic solvent, and exctacted after stirring for about 2~5 hours in extractor (20°). Nitrobenzene saturated with deionized water was used as an organic solution.

The extraction equilibrium of many salts was explained well by the law of mass action.

Dissociation and Distribution of Compounds—Dissociation and distribution of the aliphatic alkylamine-methylorange salts between two phases, the organic solvent and deionized water layers, are shown as follows;

$$MO\cdot A \rightleftharpoons A^+ + MO^- \qquad (1)$$

$$K_a = \frac{[A^+][MO^-]}{[A\cdot MO]_w} \qquad (2)$$

MO; methylorange, A; amine or ammonium compound, K_a; dissociation constant.

$$MO\cdot A_{(w)} \rightleftharpoons MO\cdot A_{(org)} \qquad (3)$$

From the Department of Pharmaceutical Analytical Chemistry, College of Pharmacy, Seoul National University, Seoul, Korea.

$$K_D = \frac{[MO\cdot A]_w}{[MO\cdot A]_o} \qquad (4)$$

K_D; distribution constant.

$[MO\cdot A]_w$; concentration of $MO\cdot A$ in the water layer.

$[MO\cdot A]_o$; concentration of $MO\cdot A$ in the N.B. layer.

Where the initial concentration of $MO\cdot A$ is $C_{MO\cdot A}$, and the extraction equilibrium is shown as equation (5) or (6).

$$C_{MO\cdot A} = [MO\cdot A]_o + [MO\cdot A]_w + [MO^-]_w \qquad (5)$$

$$C_{MO\cdot A}\cdot V_o = [MO\cdot A]_o\cdot V_o + [MO\cdot A]_w\cdot V_w + [MO^-]_w\cdot V_w \qquad (6)$$

Equation (6) is modified as the following equation;

$$\frac{C_{MO\cdot A}\cdot V_o}{\sqrt{[MO\cdot A]_o}\cdot V_w} = \sqrt{K_a\cdot K_D} + \sqrt{[MO\cdot A]_o}\left(K_D + \frac{V_o}{V_w}\right) \qquad (7)$$

or

$$\frac{V_o}{V_w}\,\frac{C_1}{[A\cdot MO]_o^{+}} = \left(\frac{K}{P}\right)^{\frac{1}{2}} + \left(\frac{1}{P} + \frac{V_o}{V_w}\right)[A\cdot MO]_o^{+} \qquad (8)$$

Dissociation constants are calculated by using the equation (8).

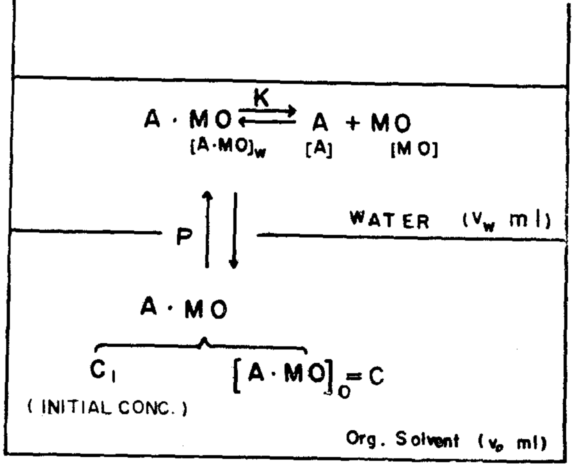


Fig. 1—Graph of dissociation and dissociation and distribution in alkylamine or alkylammonium-methylorange salt.

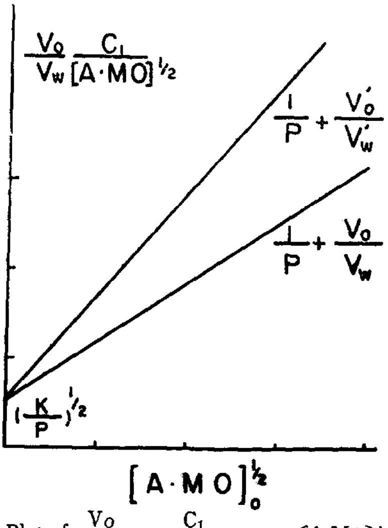


Fig. 2—Plot of $\frac{V_O}{V_W}\,\frac{C_1}{[A.MO]^{+}}$ vs. $[A.MO]^{+}$

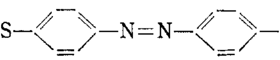
METHODS and RESULTS

Reagents and Instruments—Reagent grade *n*-alkylamine, secondary alkylamine, tertiary alkylamine (alkyl carbon number; 4, 6, 8 and 12) were used. Other reagents were distilled under vacuum. Purity of these reagents was examined by gas chromatography. A Shimadzu spectrophotometer Model QV-50 and a Taiyo Kagaku Monoshin were used. The synthesis of salts were carried out in an autoclave.

Synthesis of the primary amines-methylorange salts-1 equivalent weight of n-alkylamine (alkyl carbon number; 4, 6, 8 and 12) was placed in a 500-ml flask equipped with a mechanical stirrer. The flask was placed in an ice bath and 1.2 equivalent weight of MO solution was added with agitation thoroughly. Then, the reaction mixture was allowed to stand overnight at room temperature, and dried. The residue was recrystallized twice from absolute ethylalcohol, and dried. Purity of n-alkylamine-Mo salts was examined by gas chromatography.

The results of elemental analysis are listed in Table I.

Table I—Boiling points and reagent of elemental analysis of primary amine-methylorange salts.

Compounds	Bp	Elemental analysis (%)			
		Calcd.		Found	
		C	H	C	H
[$C_4H_9NH_3$][O_3S——$N(CH_3)_2$]	175	57.07	6.87	56.85	6.67
[$C_6H_{13}NH_3$][〃]	232	59.04	7.38	59.03	7.45
[$C_8H_{17}NH_3$][〃]	148	60.75	7.80	61.03	8.07
[$C_{12}H_{25}NH_3$][〃]	179	63.58	8.56	63.79	8.79

Synthesis of Secondary and Tertiary Amine or Quaternary Ammonium-MO Salts—14 g of Alkyl bromide (alkyl carbon number; 4, 6, 8 and 12) was placed in an autoclave equipped with a thermometer, and added 100 ml of trimethylamine solution. After addition, the reaction was continued for five hours at 80~130° under the increased pressure in an autoclave.

After reaction, the reaction material was concentrated under the reduced pressure. The residue (alkyl ammonium bromide) was recrystallized from an ethanol and ethylether mixture. Alkyl ammonium bromide was dissolved in deionized water at room temperature with stirring.

Then the proper volume of an MO solution was added to the solution. The raw materials, alkyltrimethylammonium-MO, were recrystallized from acetone, and examined by gas chromatography. Secondary and tertiary amine-MO salts were synthesized as mentioned the above. The results of elemental analysis are listed in Table II.

Extraction Conditions

Volume Ratio—The ratios of volume were differed from each other when it was extracted (Table III).

Effect of Temperature and Agitation Time—The effect of the temperature of an octylamine-MO N.B. solution, when it was extracted with deionized water, was not shown change in the range of 18~30°.

The equilibrium time between octylamine-MO N.B. solution (2×10^{-5} M) and water in the extraction procedure was approximately an hour.

Table II—Boiling points and results of elemental analysis of secondary, tertiary amine and quaternary ammonium-MO salts.

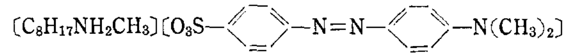
Compounds	Bp	Elemental analysis (%)			
		Calcd.		Found	
		C	H	C	H
	159°	61.57	8.08	61.41	8.13
$[C_8H_{17}NH(CH_3)_2][$ 〃 $]$	172°	62.30	8.27	62.26	8.41
$[C_{12}H_{25}NH(CH_3)_2][$ 〃 $]$	151°	64.82	8.93	65.01	8.83
$[C_4H_9N(CH_3)_3][$ 〃 $]$	279°	59.97	7.67	59.80	7.78
$[C_6H_{13}N(CH_3)_3][$ 〃 $]$	295°	61.58	8.09	61.44	8.01
$[C_8H_{17}N(CH_3)_3][$ 〃 $]$	258°	62.99	8.46	62.72	8.56
$[C_{12}H_{25}N(CH_3)_3][$ 〃 $]$	238°	65.38	9.08	65.38	9.01

Table III—Volume ratios of primary, secondary, tertiary amine and quaternary ammonium-methylorange N.B. solutions against the deionized water in the extraction procedure.

Compounds	Vol. of org. soln. (ml)	Vol. of water (ml)
n-Butylamine—MO	10	1
n-Hexylamine—MO	15	3
n-Octylamine—MO	10	10
n-Laurylamine—MO	5	10
Octylmethylamine—MO	10	10
Octyldimethylamine—MO	5	5
Lauryldimethylamine—MO	1	10
Buthyltrimethylammonium—MO	10	5
Hexyltrimethylammonium—MO	10	10
Octyltrimethylammonium—MO	3	15
Lauryltrimethylammonium—MO	1	10

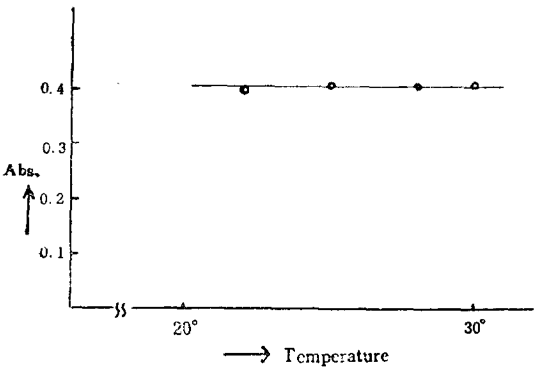


Fig. 3—Effect of temperature of octylamine-MO N.B. soln. in the extraction procedure.

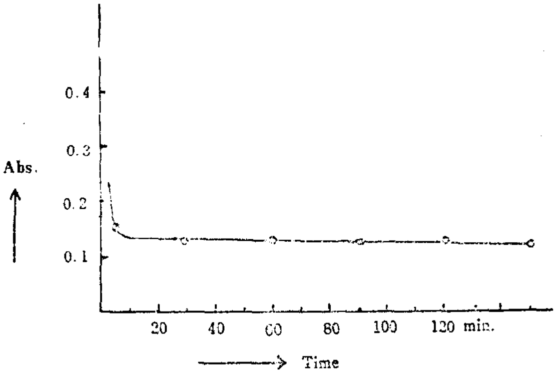


Fig. 4—Time of extraction equilibrium in octylamine-MO N.B. soln. (2×10^{-5} M)(λ_{max}: 431 nm, 20°)

Maximum Absorption Wavelength and Absorption Coefficient of Salts—A control solution of primary, secondary, tertiary amine-MO and quaternary ammonium-MO salts (1×10^{-5}—5×10^{-5} M), were used in the measurement of absorbance of salts, and the calibration curve or absorption coefficient was determined by the measurement of absorbance in the maximum wavelength absorption. The results of the measurement are listed in Table IV.

Table IV—Absorption maximum wavelength, calibration curve and absorption coefficient of salts.

Compounds	Max. absorp.wave(nm)		Calib. curv		Absorp. co.
	org. soln.	water	org. soln.	water	org. soln. ($\times10^5$)
Butylamine—MO	430	466	$y=0.240x$	$y=0.276x$	0.241
Hexylamine—MO	431	466	0.251	0.277	0.252
Octylamine—MO	432	466	0.252	0.270	0.252
Laurylamine—MO	430	466	0.255	0.264	0.258
Octylmethylamine—MO	432	466	0.257	0.275	0.258
Octyldimethylamine—MO	433	466	0.250	0.268	0.257
Lauryldimethylamine—MO	430	466	0.260	0.267	0.263
Buthyltrimethylammonium—MO	430	466	0.266	0.280	0.266
Hexyltrimethylammonium—MO	432	466	0.263	0.275	0.263
Octyltrimethylammonium—MO	434	466	0.266	0.269	0.266
Lauryltrimethylammuonim—MO	431	466	0.271	0.273	0.269

Calculation of Distribution Coefficient and Recovery Ratio—A proper volume of primary, secondary, tertiary amine-MO and quaternary ammonium-MO N.B. solutions was added to a proper volume of deionized water, and stirring was continued at 20° for 2 to 5 hrs.

After extraction, the absorbance of the organic and water layers was measured at 430～434nm and 466 nm by using a spectrophotometer, respectively.

The square root of the concentration of salts was plotted against the initial concentration per the square root of the concentration salts after extraction.

The graph represented straight lines. The recovery ratio (R.R.) was given as follows;

$$R.R.=\frac{(MO.A)_o\cdot V_o/1000+(MO.A)_w\cdot V_w/1000}{(C_I)\cdot V_o/1000}$$

The results are listed in Table V.

Relation of Distribution Coefficient and Volume Ratio—When plotting the concentration of N.B layer against using Equation 7, the straight line was obtained.

In the case of left-hand graph, the value of intercept in almost the same when the volume ratio is changed from 10 : 3 to 10 : 5, and the value of the distribution constant is 1.25 or 1.42.

In the right-hand graph, the value of intercept is differed by changing the volume ratio,

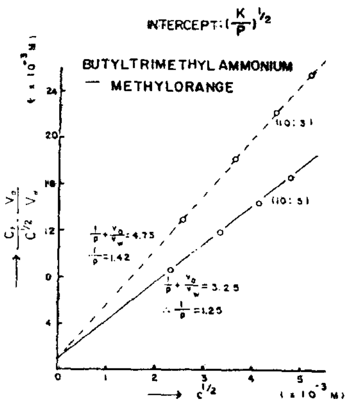
Table V—Equation, recovery ratio and distribution coefficient of salts after extraction.

Compounds	Equation			R.R.	K_D
Butylamine—MO	$y=0.352x$	+	0.293×10^{-2}	98.4	25.20
Hexylamine—MO	0.262		0.181	99	8.09
Octylamine—MO	0.235		0.233	97.2	1.35
Laurylamine—MO	0.126		0.07	99.5	0.13
Octylmethylamine—MO	0.143		0.146	94.2	0.43
Octyldimethylamine—MO	0.124		0.031	97	0.24
Lauryldimethylamine—MO	0.118		0.048	95.8	0.02
Butyltrimethylammonium—MO	0.162		0.052	96	1.24
Hexyltrimethylammonium—MO	0.132		0.038	101	0.32
Octyltrimethylammonium—MO	0.147		0.029	102	0.01
Lauryltrimethylammonium—MO	0.111		0.005	99.6	0.01

but the value of the distribution constant is well coincident. In general, the reappearance of the intercept is not so good as compared to that of the slope.

Relation of the Concentration and Conductivity— In order to know the extractability of the amines and ammonium salts, experiments were performed as the mentioned the above procedure. The results are shown in Fig. 5, 6 and 7.

The linear relationship between the concentration and the conductivity of the compounds was shown.



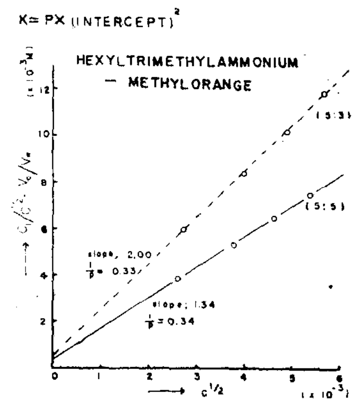


Fig. 5—Plot of $C_1/C^+ \cdot V_o/V_w$ vs. C^+ (BTA·MO). **Fig. 6**—Plot of $C_1/C^+ \cdot V_o/V_w$ vs. C^+ (HTA·MO).

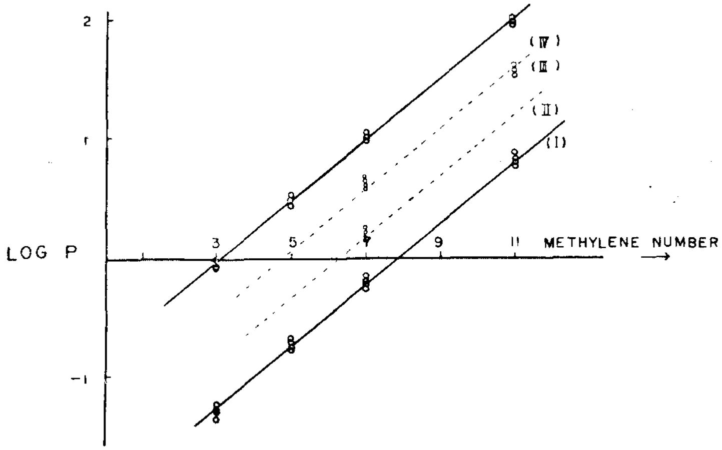


Fig. 7—Plot of logarithm of distribution coefficient against methylene numbers of alkyl radicals.

DISCUSSION

The order of extraction for primary amine, secondary amine, tertiary amine-MO and quaternary ammonium-MO salts by using the organic solvent are decreased as follows:

Quaternary-> Tertiary-> Secondary-> Primary-

and the length of alkyl radicals for all salts arranged in the decreasing order of K_D:

Lauryl-> Octyl-> Hexyl-> Butyl-

As can be seen in Fig 5 and 6, the extraction of the quaternary ammonium- MO salts in the water layer is more difficult than that of primary amine-MO salts, and when the number of alkyl radicals increases in the same salts, it is also difficult to extract in the water layer. The alkyl carbon number is not always dependent upon the absorbance, and the differences of absorption coefficient among primary amine, secondary amine, tertiary amine and quaternary ammonium-MO salts are not so large. The logarithm of distribution coefficient against the methylene number in all primary, secondary, tertiary amines and quaternary ammonium-MO salts was the straight lines.

REFERENCES

1. B-K Kim, *Spectrochim. Acta*, in press (1974)
2. *Ibid., Bull. Chem. Soc. Japan*, **48**, 78 (1974)
3. *Ibid.*,, in press (1974)
4. *Ibid.*, in press (1974)
5. *Ibid, J. Pharm. Soc. Korea.*, in press (1974)
6. R. L. Reeves and R. S. Kaiser, *Can. J. Chem.*, **51**, 628 (1973)
7. F. Quadrifoglio and V. Crescenzi, *J. Colloid and Inter. Sci.*, **35**, 447 (1971)
8. N. A. Gibson and D. C. Weatherburn, *Anal. Chim. Acta*, **58**, 149 (1972)
9. *Ibid*, **58**, 159 (1972)