[CONTRIBUTION FROM THE RESEARCH DIVISION OF ARMOUR AND COMPANY]

Conductometric Studies of Solubility and Micelle Formation[1]

BY D. N. EGGENBERGER AND H. J. HARWOOD

Conductometric studies over a range of temperatures were made on solutions of a substance, dodecylammonium chloride, whose critical concentration is in the region of saturation. Plots of specific conductance *vs.* normality demonstrate the conducting property of the micelle as contrasted with the non-conducting property of the precipitate (dodecylammonium chloride hemihydrate). Temperature *vs.* square root of normality plots of critical points and precipitation points show that the two curves intersect at the sharp break in the precipitation curve. This break is attributed to the "Krafft effect," thus substantiating the interpretation that this phenomenon is the result of solubilization of undissociated molecules by the micelle.

Conductance techniques have been applied to the determination of the solubility of higher alkyl quaternary ammonium salts of fatty acids.[2] The conclusions reported were based on the assumption that the critical concentration of a cationic colloidal electrolyte is a measure of the solubility of the compound. Subsequent solubility studies on a series of the N-methyldodecylammonium chlorides[3] whose critical points are close together[4] have demonstrated that no direct relationship between solubility and critical point is evident. The present investigation was undertaken in an attempt to throw further light on the relation of micelle formation to solubility in solution of a substance, dodecylammonium chloride, whose critical concentration is in the region of saturation. This work involved conductance measurements on varying concentrations of the salt over the temperature range 0 to 60°.

Experimental

Preparation of the dodecylammonium chloride has been previously described.[5] Techniques employed in making the conductance measurements were described in an earlier publication from this Laboratory.[2] In order to obtain uniform accuracy over a wide range of concentrations, resistance measurements were made in a series of four cells with various constants (13.359, 2.1503, 0.4678, 0.08792). These cells were connected by 2-mm. glass tubing and all joints were sealed to prevent loss or contamination of the solution. The solution under investigation was passed into that cell having the constant appropriate for the particular concentration.

Measurements on solutions in which precipitation occurred were repeated until constant values were obtained. In solutions whose concentration was above the critical point this usually required a period of hours, in some cases extending overnight.

Results and Discussion

Conductance data are frequently plotted as equivalent conductance *vs.* the square root of normality. Such plots, which are linear for simple, completely dissociated electrolytes in diluted solution, permit the approximation of the limiting conductance at infinite dilution. In the case of colloidal electrolytes, in which an abrupt change in conductance occurs at the critical concentration, equivalent conductance plots give an exaggerated and distorted picture of the effects. In fact, such breaks in equivalent conductance plots which are the result of micelle formation are not readily distinguished from breaks occurring as the result of precipitation. Accordingly, the significant findings in the present work are presented as specific conductance *vs.* normality plots.

In Table I are given specific conductance data for dodecylammonium chloride at 0, 10, 15, 20, 25, 27, 30, 40, 50 and 60°. Values in parentheses represent measurements on freshly prepared supersaturated solutions. Other conductance values are those obtained at equilibrium. For purposes of discussion, conductance values at 27 and 15° are plotted in Figs. 1 and 2. In each plot, A represents the critical point and B the precipitation point. Line AC represents conductance of solutions containing micelles and BD of solutions containing crystals (dodecylammonium chloride hemihydrate). At 15° the critical concentration is observed in the supersaturated solution.

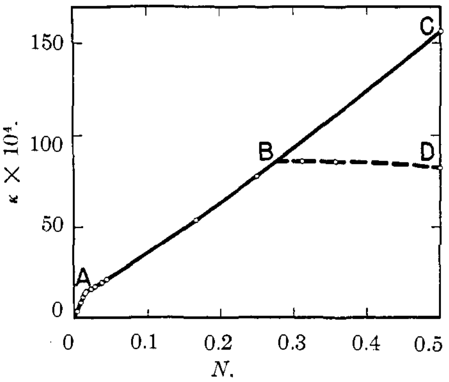

Fig. 1.—Specific conductance of dodecylammonium chloride in water at 27°.

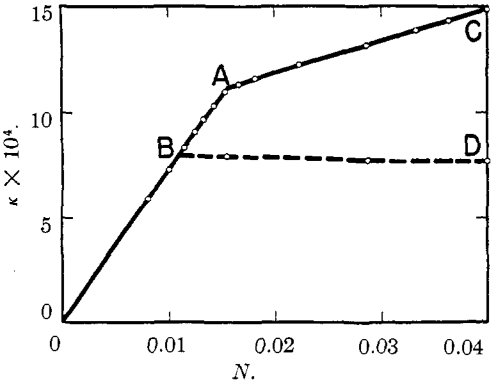

Fig. 2.—Specific conductance of dodecylammonium chloride in water at 15°.

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[1] Presented before the Division of Physical and Inorganic Chemistry at the Chicago Meeting of the American Chemical Society, September, 1950.

[2] D. N. Eggenberger, F. K. Broome, R. A. Reck and H. J. Harwood, THIS JOURNAL, **72**, 4135 (1950).

[3] F. K. Broome, C. W. Hoerr and H. J. Harwood, *ibid.*, **73**, 3350 (1951).

[4] A. W. Ralston, F. K. Broome and H. J. Harwood, *ibid.*, **71**, 671 (1949).

[5] A. W. Ralston and D. N. Eggenberger, *ibid.*, **70**, 436 (1948).

TABLE 1

SPECIFIC CONDUCTANCE OF DODECYLAMMONIUM CHLORIDE

0°		10°		15°		20°		25°	
N^a	$\kappa \times 10^4$	N^a	$\kappa \times 10^4$	N^a	$\kappa \times 10^4$	N^a	$\kappa \times 10^4$	N^a	$\kappa \times 10^4$
0.000980	0.503	0.000490	0.333	0.00801	5.89	0.000507	0.444	0.000777	0.746
.002381	1.196	.001190	.805	.01001	7.31	.001267	1.096	.001773	1.688
.004545	1.958	.00227	1.517	.01144	(8.30)	.00284	2.42	.00398	3.70
.00763	(3.14)	.00455	2.99	.01251	(9.05)	.00402	3.40	.00871	7.92
.01154	2.72^b	.00648	4.15	.01334	(9.64)	.00635	5.27	.01025	9.31
.01296	2.71^b	.00833	5.31	.01430	(10.30)	.00934	7.63	.01558	13.50
.01429	2.70^b	.00985	(6.28)	.01540	(10.98)	.01025	8.34	.0223	15.26
.01875	2.66^b	.01154	(7.32)	.01552	7.90^b	.01500	10.43^b	.0437	19.97
.02222	2.64^b	.01296	(8.10)	.01668	(11.32)	.01700	(12.60)	.0714	26.8
		.01429	(8.87)	.01820	(11.59)	.01813	(12.74)	.0769	27.9
		.01667	5.51^b	.02224	(12.21)	.0208	(13.34)	.0100	(34.1)
		.0197	5.48^b	.02859	(13.15)	.0265	(14.37)	.0100	32.7^b
		.0222	5.42^b	.02870	7.73^b	.0484	(18.44)	.1371	(43.4)
				.03336	(13.86)	.0782	(24.4)		
				.03639	(14.31)	.1397	(37.5)		
				.04003	(14.86)				
				.04003	7.71^b				

27°		30°		40°		50°		60°	
N^a	$\kappa \times 10^4$	N	$\kappa \times 10^4$	N	$\kappa \times 10^4$	N	$\kappa \times 10^4$	N	$\kappa \times 10^4$
0.00385	3.77	0.000985	1.048	0.000801	1.023	0.000968	1.439	0.000905	1.558
.00909	8.65	.001789	1.896	.001857	2.34	.00213	3.13	.001936	3.28
.01228	11.55	.00335	3.51	.00405	5.03	.00445	6.48	.00466	7.77
.01379	12.81	.00617	6.34	.00728	8.96	.00820	11.68	.01115	18.01
.01453	13.42	.00850	8.66	.00806	9.80	.00933	13.22	.01433	23.02
.01525	13.87	.01155	11.60	.01455	17.43	.01417	19.93	.01800	27.92
.01667	14.39	.01354	13.64	.01768	18.95	.01813	23.3	.0248	32.2
.02308	15.94	.01726	15.62	.0208	20.03	.0223	25.1	.0439	42.1
.02857	17.28	.02264	17.10	.0288	23.1	.0241	26.3	.0729	58.1
.03750	19.34	.03844	21.12	.0480	29.7	.0423	34.1	.1345	95.4
.04444	21.11	.0622	27.64	.0796	41.5	.0682	45.7		
.1667	53.7	.1008	39.04	.1353	63.9	.1383	80.9		
.250	77.4	.1493	54.3						
.312	85.9^b								
.357	85.7^b								
.500	(157.1)								
.500	82.2^b								

[a] N indicates "gross normality" including precipitated solid. [b] Precipitate present.

Two significant features of these curves deserve comment. The continuation of the almost linear rise in conductance beyond the critical concentration indicates the continued formation of conducting particles of uniform or at least uniform average size. This conducting property of the micelle is contrasted with the non-conducting property of the precipitate. Solutions containing the latter exhibit slightly decreasing conductance with increasing concentration, as might be expected where an increasing number of non-conducting particles are appearing.[6]

Plots of conductance values obtained at the various temperatures employed may be considered as falling into four categories. At 0 and 10° precipitation was observed. Some supersaturation occurred but in neither case was the critical concentration reached. At 15 and 20° the critical concentration was observed in the supersaturated solution. At 25 and 27° the precipitation point was above the critical concentration. At 30, 40, 50 and 60° no precipitation occurred within the range of concentrations studied.

The critical points and precipitation points for solutions of dodecylammonium chloride over the range of temperatures studied are given in Table II and are plotted in Fig. 3 as temperature *vs.* square root of normality. (Lines EF and FG represent precipitation of dodecylammonium chloride hemihydrate.) (Values obtained by the conductometric method are somewhat lower than those obtained by

TABLE II

CRITICAL AND PRECIPITATION POINTS FOR DODECYLAMMONIUM CHLORIDE SOLUTIONS

T	Critical point	Precipitation point
0	....	0.0060
10	....	.0088
15	0.0156	.0110
20	.0156	.0145
25	.0152	.097
27	.0150	.277
30	.0150	
40	.0149	
50	.0165	
60	.0180	

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(6) Although the effects are somewhat confused by the presence of sodium and chloride ions, conductance data for the higher alkyl quaternary ammonium salts of fatty acids (ref. 2), when examined in light of the present findings, definitely indicate that the breaks are the result of precipitation rather than of micelle formation.

visual observation.[3]) The point F corresponds to a sharp break in the curve and is attributed to the "Krafft effect" or solubilization of the undissociated molecule by the micelle. Significantly the critical-point curve HFI intersects the precipitation curve at this point. The portion of this curve FI represents critical points as observed in supersaturated solution. Point F occurs at a temperature very near 23° and at a concentration of 0.015 *N*. The very sharp break in the precipitation curve at point F can be interpreted as indicating no appreciable formation of micelles below the critical concentration.

The slowness with which precipitation occurred in solutions whose concentration was above the critical point can be explained on the basis that orientation in the micelle is tail-to-tail, whereas in dodecylammonium chloride (and probably in the hemihydrate) it is head-to-tail.[7] Conversion of micelle to crystal would thus involve passage of the individual molecule through the solution phase.

The portion of the precipitation curve to the left of E, the eutectic at 0.006 *N*, represents the liquidus along which ice separates.

The fact that the critical concentrations pass through a minimum with respect to temperature has been observed with other colloidal electrolytes.[8]

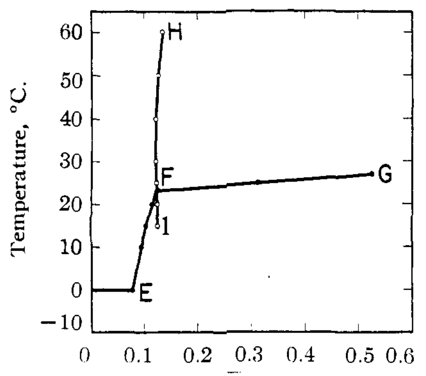

Fig. 3.—Critical points and precipitation points for aqueous solutions of dodecylammonium chloride.

Although no generalizations can be drawn, it appears evident that with dodecylammonium chloride in the range of concentrations studied micelle formation is the result of ionic aggregation plus solubilization of undissociated molecules. Further work will be directed toward a study of such solubilization and its influence on the properties of the solution.

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[7] C. R. Hudgens, Abstract of Thesis, University of Illinois, 1950.

[8] A. P. Brady and H. Huff, *J. Colloid Sci.*, **3**, 511 (1948).

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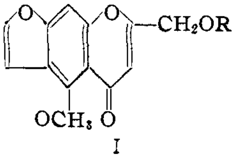
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

Chromones. IV. The Conversion of Khellol into Visnagin. Derivatives of Khellol and Visnagin

BY T. A. GEISSMAN

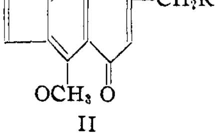
A number of derivatives of visnagin and khellol have been prepared for physiological studies. Khellol tosylate is a convenient intermediate for the preparation of some of these derivatives; and, in particular, by conversion into the iodo compound, followed by reduction of the latter, offers a practical means for converting khellol into visnagin.

Of the three known furochromones present in the fruit of *Ammi visnaga*, khellol glucoside (I, R = $C_6H_{11}O_5$) is the most abundant.[1] While khellin, and to a lesser degree visnagin, shows therapeutic promise as a smooth muscle relaxant and coronary dilator,[2] the glucoside and the aglucone, khellol, are pharmacologically ineffective in these respects. Because of the possibility that compounds derived from khellol might prove to have physiological activity, and thus that the readily available glucoside would serve as a source of therapeutically useful khellin-like substances, a number of derivatives of khellol and visnagin were prepared for pharmacological studies.

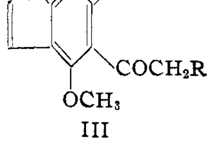


I

These compounds were prepared in two ways: (1) by replacement of the hydroxyl-hydrogen atom of khellol (I, R = H) by a series of acyl residues; and (2) by the synthesis of chromones of the general structure II by partial synthesis starting from visnaginone[1b] (III, R = H) and by replacement of the hydroxyl group of khellol.



II



III

Khellol tosylate (I, R = *p*-toluenesulfonyl) proved to be of particular interest. It can be readily prepared in excellent yield; the replacement of the tosyloxy group provides a route to 2-methyl-substituted derivatives of visnagin; and it afforded a simple and effective means of converting khellol into visnagin. Reaction of the tosylate with sodium iodide and with aniline led, respectively, to II (R = I) and II (R = NHC_6H_5). When the iodo compound was treated with zinc dust in acetic acid, visnagin (II, R = H) was formed smoothly and in good yield. The same over-all result can be

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[1] E. Späth and W. Gruber, (a) *Ber.*, **71**, 106 (1938); (b) **74**, 1492 (1941); (c) **74**, 1541 (1941).

[2] See G. V. Anrep, G. S. Barsoum and M. R. Kenawy, *Am. Heart J.*, **37**, 531 (1949).