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

Carbonyl Reactions. V. Acidity and Temperature Dependence in the Condensation of Anisaldehyde and Methyl Ethyl Ketone[1]

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The acidity dependence of the rate of condensation of anisaldehyde and methyl ethyl ketone has been measured in acetic acid–sulfuric acid medium. Dependence upon the relative activity of water has been determined. Further evidence in support of the mechanism outlined is adduced.

Introduction

In the previous paper of this series it was established that the sequence of reactions leading to the formation of 4-*p*-anisyl-3-methyl-3-buten-2-one (III) in acetic acid involves important kinetic roles for the intermediate β-hydroxyketone and its acetate ester.[2]

It is the purpose of the present report to investigate the dependence of the various steps upon acidity, and to seek further confirmation for the reaction mechanism put forth previously.

Hammett has defined an acidity function H_0 for strong acids in aqueous solution in terms of acid-base equilibria of uncharged bases such as aniline.[3] The acidity function is a property of solvent composition only when the activity coefficient relationship holds

$$f_B/f_{BH^+} = f_C/f_{CH^+} \qquad (1)$$

where C represents any uncharged base other than B. This relationship appears to hold reasonably well over wide concentration ranges in various strong acid solutions. H_0 has been used extensively to measure the basicity of weak bases[4] but its most important application has been in the field of reaction kinetics.[5] The extension of the acidity function to mixed and non-aqueous solvent systems has received considerable attention. Measurements of H_0 have been made in numerous solvent systems other than water–strong acid,[4] but any demonstration of the constancy of the activity coefficient ratios in general has not been presented.[6]

It has been shown recently that the enolization of acetone closely parallels the measured acidity function in mixed ethanol–water solvents of high ethanol content.[7] Satchell has suggested that the variation of reaction rate with increasing acid concentration in such largely non-aqueous solvents will be inadequate for diagnostic purposes.

The situation in acetic acid as a solvent is by no means straightforward. It previously has been observed by Paul and Hammett[8] that the rate of halogenation of nitroacetophenone parallels the measured acidity function in acetic acid, but with a slope of 1.4.

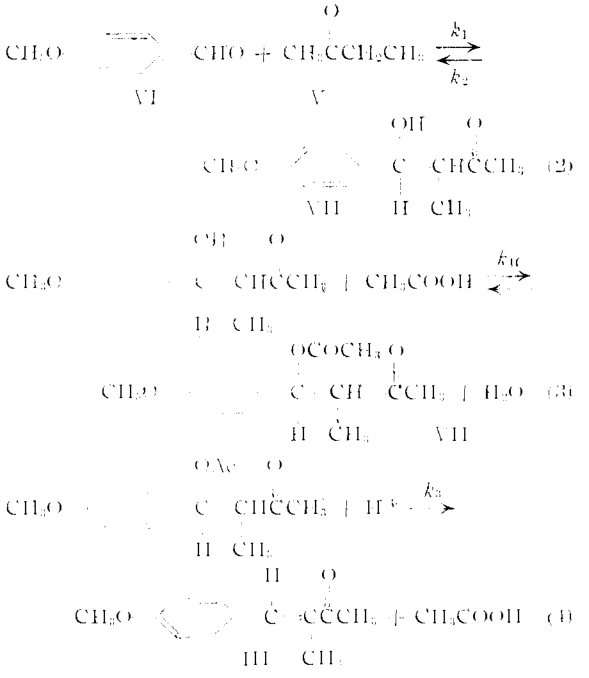
Noyce and Pryor[9] observed that the measured rates of condensation of benzaldehyde and acetophenone parallel the measured acidity function in acetic acid, and Gebhart and Adams have observed similar results on the rearrangement of benzopinacol.[10]

Experimental

The procedures used have been described previously.[2,9] Most rate measurements were carried past 50% reaction. Where two competing reactions have been measured, infinity readings have also been used in calculating rate constants.

Discussion

The reaction sequence outlined in the preceding paper is used here for the following discussion.



The Dependence of the Final Elimination Step, k_3, upon the Acidity. Since it has been established that the rates of esterification and hydrolysis for the β-hydroxyketone and its ester are rapid relative to the other reaction steps, it is straightforward to measure the rate of formation of 4-(*p*

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[1] Supported in part by the Office of Ordnance Research Contract No. DA-04-200-ORD-171.

[2] D. S. Noyce and L. R. Snyder, THIS JOURNAL, **80**, 4033 (1958).

[3] L. P. Hammett and A. J. Deyrup, *ibid.*, **54**, 2721 (1932).

[4] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 273–276; M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

[5] F. A. Long and M. A. Paul, *ibid.*, **57**, 935 (1957).

[6] Hammett's justification for the identity $f_B/f_{BH^+} = f_C/f_{CH^+}$ in water–strong acid solutions is based upon the observed dependence of similar activity coefficients on the dielectric constant of the solution; this dependence is of the form

$$f_B/f_{BH^+} = a + b/D$$

and b is usually of such magnitude that in solutions of high dielectric constant, b/D is essentially zero.

[7] D. P. N. Satchell, *J. Chem. Soc.*, 2872 (1957).

[8] M. A. Paul and L. P. Hammett, THIS JOURNAL, **58**, 2182 (1936).

[9] D. S. Noyce and W. A. Pryor, *ibid.*, **77**, 1397 (1955).

[10] H. J. Gebhart, Jr., and K. H. Adams, *ibid.*, **76**, 3925 (1954).

anisyl)-3-methyl-3-butene-2-one (III) from the intermediate ester. In anhydrous acetic acid the elimination reaction can involve only the ester, and proceeds to completion; in wet acetic acid incursion of the cleavage reaction (k_2) becomes important. The measured rates of elimination are summarized in Table I.

TABLE I

RATE OF FORMATION OF 4-*p*-ANISYL-3-METHYL-3-BUTENE-2-ONE[a]

Initial concentrations H$_2$SO$_4$, M	H$_2$O, %	VII × 10^2 M	$k_3 \times 10^5$, sec.$^{-1}$	H_0[b]	log $k_3 + H_0$
0.200	0.96	1.61	3.25	−1.58	−6.07
.200	.96	2.77	3.30	−1.58	−6.06
.400	.96	0.840	11.22	−2.07	−6.02
.600	.96	2.20	23.4	−2.38	−6.00
.800	.96	4.14	44.2	−2.61	−5.96
.800	.96	2.43	43.1	−2.61	−5.97
1.00	.96	2.78	65.8	−2.79	−5.97
1.00	.96	2.99	65.0	−2.79	−5.98
0.200	.70	2.44	4.47	−1.70	−6.05
.200	.45	2.76	5.50	−1.81	−6.07
.200	.20	2.19	6.94	−1.92	−6.08
.200	.02	1.78	8.03	−1.94	−6.03
.200	.02	3.46	7.72	−1.94	−6.05
.600	.00	2.06	44.6	−2.65	−6.00
1.000	.00	1.85	109	−2.98	−5.94

[a] Solvent acetic acid; temperature 25.14°. [b] Values of the acidity function H_0 in acetic acid–sulfuric acid mixtures containing varying amounts of water were interpolated from the data of Gold and Hawes.[11] Although Gold and Hawes' water concentrations are relative to a small unknown initial water content, this has been estimated by comparison with other data.[12]

The average value for log $k_3 + H_0$ of Table I is -6.02 ± 0.04 and this correlation is considered satisfactory. The best slope through the data is -1.08. A most significant feature of the data in Table I is the conclusive demonstration that k_3 is a function of the acidity only, and is independent of the water concentration. The elimination reaction in anhydrous acetic acid must involve only the acetate; the elimination reaction in the aqueous acetic acid solutions used proceeds from an equilibrium mixture of the ester and alcohol, containing only minor amounts of the alcohol. Under these conditions it would be coincidental for the rates of elimination from the alcohol and the ester to be identical. It may be concluded then that the elimination process proceeds from the ester alone.

The Condensation Step, k_1.—The true rate constant for the condensation step has been obtained by two methods. For solutions containing water, k^0_1 is calculated from the measured values of k', k_2 and k_3 as described earlier.[2] In anhydrous solutions, however, k_2 becomes zero, and the direct measurement of the rate of disappearance of anisaldehyde is possible. The rate data of Table II were obtained by these processes.

With the exception of the kinetic experiments at 1.00 molar sulfuric acid in solutions containing 0.96 % water, good correlation with the acidity function is obtained (log $k_1^0 + H_0 = 5.89 \pm 0.02$). It is possible that altered rates of esterification and hydrolysis, at the higher acid concentration, now render unsuitable the simple mathematical treatment with three rate-controlling processes involved, which has been used.

TABLE II

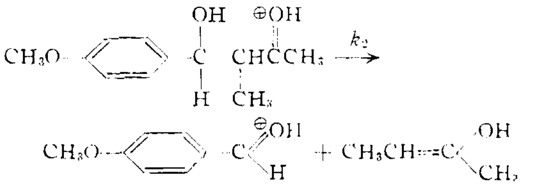
RATE OF CONDENSATION OF ANISALDEHYDE (VI) AND METHYL ETHYL KETONE

H$_2$SO$_4$ concn.	VI concn. × 10^3	$k' \times 10^5$ sec.$^{-1}$	$k_1^0 \times 10^5$ l mole^{-1} sec.$^{-1}$	H_0	log $k_1^0 + H$
(a) Initial concentrations: water, 0.96%; methyl ethyl ketone, 0.300 M					
0.400[a]			14.2 ± 0.2	−2.07	−5.92
.600	2.66	5.61	30.6	−2.38	−5.89
.600	2.66	5.64	30.7	−2.38	−5.89
1.00	2.66	14.8	63.9	−2.79	−5.98
1.00	2.66	14.0	61.1	−2.7	−6.00
1.00	4.50	14.33	62.5	−2.79	−5.99
(b) Initial concentrations: water, 0.02%; methyl ethyl ketone, 0.159 M					
0.224	2.45		13.4	−2.01	−5.88
.369	2.45		28.1	−2.33	−5.88
.800	2.45		89.7	−2.83	−5.88
.800	2.45		91.4	−2.83	−5.87

[a] Average value from previous papers.[2]

The direct formation of the intermediate acetate from anisaldehyde and methyl ethyl ketone would involve the activity of water entering the rate expression. There is no evidence for any such dependence for k_1. It is thus considered likely that the mechanism of the condensation step involves the reaction between the enol of methyl ethyl ketone and the protonic salt of anisaldehyde.[9,13]

The Reverse Aldol Step, k_2.—If the conclusions on the mechanism of the k_1 or condensation step be correct, the mechanism of the k_2 or reverse aldol step, by the principle of microscopic reversibility, must be as represented in equation 5.



(5)

The intermediate alcohol, however, is in equilibrium with the intermediate acetate and is present to the extent of only a few per cent. In aqueous acetic acid, measured rates have been obtained in almost all cases by starting with the acetate; it can be shown then that the rate dependency should be of the following form, as solution composition is varied from 0.2-1.0 molar sulfuric acid and 0-

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[11] V. Gold and B. W. V. Hawes, *J. Chem. Soc.*, 2102 (1951).

[12] N. F. Hall and W. Spengeman, THIS JOURNAL, **62**, 2487 (1940); T. L. Smith and J. H. Elliot, *ibid.*, **75**, 3566 (1953).

[13] Long and Paul[5] have questioned the significance of the observed correlation with H_0 obtained by Noyce and Pryor for the similar reaction step in the condensation of acetophenone and benzaldehyde. However, such a correlation would appear to be expected. An acid-catalyzed cleavage reaction involving the fragmentation of the organic moiety as its protonic salt would be expected to show correlation with the acidity function. By the principle of microscopic reversibility, the condensation reaction should likewise show correlation with the acidity function. Recently Deno, Edwards and Perizzolo[14] have observed good correlation of the second-order rate coefficient for the reaction between *t*-butyl alcohol and acrylonitrile with h_0.

[14] N. C. Deno, T. Edwards and C. Perizzolo, THIS JOURNAL, **79**, 2108 (1957).

1% water

$$k_2/h_0 = k_2^0 K_H[f_{VII}/f_{VIII}a_{HAc}]/[a_{H_2O}] \quad (6)$$

where h_0 is antilog $-H_0$, K_H is the equilibrium constant for the ester hydrolysis and the activities and activity coefficients have their usual significance. The activity coefficients of the neutral species would not be expected to vary markedly; the activity of acetic acid is nearly constant, and hence variation of rate should parallel the activity of water and the acidity in the medium.

TABLE III

RATE OF REVERSAL OF CONDENSATION AS A FUNCTION OF ACID AND WATER CONCENTRATION[a]

H_2O, %	H_2SO_4, M	$k_2 \times 10^5$ sec.$^{-1}$	H_0	a_{H_2O} calcd.[b]	a_{H_2O} from gold
0.95	0.200	3.52	−1.58	(1.00)	(1.00)
.96	.400	7.75	−2.07	0.70	0.38
.96	.600	11.3	−2.38	.51	.20
.96	.800	14.6	−2.61	.38	.11
.96	.800	14.4	−2.61	.38	.11
.96	1.00	16.5	−2.79	.28	.07
.70	0.200	3.50	−1.70	.74	.69
.45	.200	2.76	−1.81	.46	.46
.200	.200	1.43	−1.92	.19	.21

[a] Concentration VI 0.005–0.05 M in various runs; duplicates agreed to ±3% in all cases; solvent acetic acid; temperature 25.14°. [b] Calculated by eq. 7.

It is possible to estimate the relative activities of water in the various solutions used from the data of Gold and Hawes.[11]

Qualitatively, the activity of water calculated from the rate data, on the assumption that

$$\log k_2 + H_0 - a_{H_2O} = \text{constant} \quad (7)$$

is seen to parallel the relative activities of water calculated from Gold's data. Quantitative agreement is, however, lacking as the sulfuric acid content is varied. On the other hand, a remarkably satisfactory correlation results at one sulfuric acid concentration as the water concentration is varied. The evidence thus obtained from the acid variation on the reversal of the condensation step is consistent with the mechanism represented by equation 5.

It is also to be noted that these conclusions strengthen the earlier results and expectation that condensation of two neutral species should be correlatable with the acidity function. It would not be expected that the activity coefficients of substances such as methyl ethyl ketone and of anisaldehyde would change with the acidity of the medium to any appreciable extent, and that therefore the cancellation of activity coefficient terms as proposed by Noyce and Pryor[9] is reasonable.

Dehydration and Reversal in Aqueous Solvents.—To gain further insight into the role of acid catalysis in the total reaction picture, we have examined the dehydration reaction in aqueous sulfuric acid, where the utility of H_0 is well accepted, and questions of interpretation are much less fraught with difficulty and ambiguity. The results are presented in Table IV.

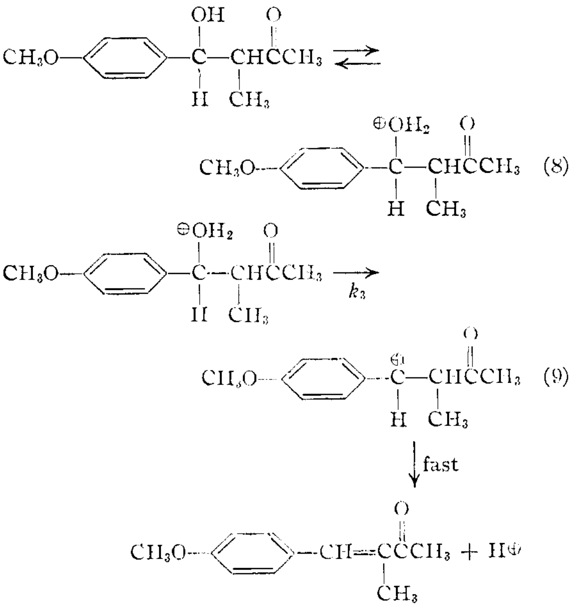
TABLE IV

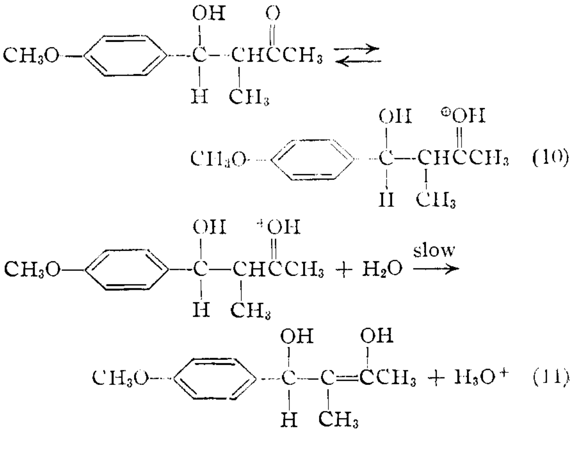
DEHYDRATION AND REVERSAL IN AQUEOUS SULFURIC ACID[a]

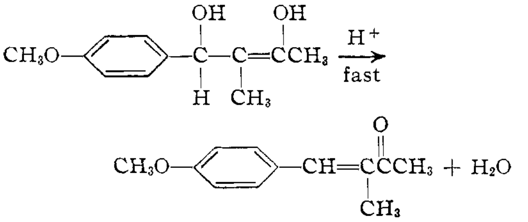
H_2SO_4, M	VII $\times 10^3$ M	$k_2 \times 10^5$ sec.$^{-1}$	$k_3 \times 10^5$ sec.$^{-1}$	H_0	log $k_2 + H_0$	log $k_3 + H_0$
3.52	1.15	2.36	1.58	−1.63	−6.26	−6.43
3.52	1.15	2.55	1.67	−1.63	−6.23	−6.41
4.25	1.23	4.75	3.08	−1.95	−6.27	−6.46
4.25	1.06	5.06	3.28	−1.95	−6.24	−6.43
5.29	1.22	14.4	10.4	−2.40	−6.24	−6.38
5.29	1.16	14.4	10.4	−2.40	−6.24	−6.38
6.16	1.21	31.2	29.0	−2.85	−6.35	−6.39
7.07	3.05	73.1	105	−3.37	−6.50	−6.35
7.07	2.90	68.9	97.0	−3.37	−6.53	−6.39
7.07	2.77[b]	74.1	93.6	−3.37	−6.50	−6.40
8.08	2.84	170	330	−3.91	−6.68	−6.39
					Av. 6.40 ± 0.02	

[a] Temperature 25.00°. [b] Using the alcohol VIII instead of the ester VII.

The correlation of the rate of elimination with H_0 in aqueous sulfuric acid should be compared with the rate of elimination in sulfuric acid–acetic acid solutions. Complete parallelism of behavior with respect to changing acidity is observed. We conclude that this evidence strongly supports a direct elimination reaction under these conditions. This mechanism outlined in equations 8 and 9 is to be contrasted with a possible mechanism which we wish to rule out in this instance, involving enolization as the rate-controlling process (equations 10–12). Evidence to be presented in a succeeding







(12)

paper[15] indicates that under certain circumstances, enolization does in fact represent an important reaction path for the dehydration of β-hydroxyketones.

Temperature Coefficients.—The temperature coefficients for the various reaction processes discussed above have been measured. The data are presented in Table V.

As expected, the entropy of activation for the condensation step, k_1^0 (calculated to H_0 of zero), is far smaller than that of the various other steps because of the larger molecularity of this particular reaction relative to the others. The addition of another neutral molecule to an activated complex usually subtracts about 15 entropy units of translational entropy from the entropy of activation in aqueous solution[16]; the same phenomenon in organic solvents is attended by a decrease in the entropy of activation of about 25–28 entropy units. It is seen that the entropy of activation for the condensation step, k_1^0, is reasonable.

TABLE V

TEMPERATURE COEFFICIENTS FOR REACTION STEPS

Reaction conditions	T, °C.	$k_1^0 \times 10^5$ l. mole^{-1} sec.$^{-1}$	$k_2 \times 10^5$ sec.$^{-1}$	$k_3 \times 10^5$ sec.$^{-1}$
VII in anhyd.	25.15			See Table I
acetic acid;	35.39			24.8
0.2 *M* sul-	35.39			24.9
furic acid	45.51			71.1
	45.51			72.9
	54.28			170
$\Delta H^{\pm}$				20.2 kcal.
$\Delta S^{\pm}$				−11 e.u.
VII in acetic	25.15	14.2	7.75	11.22
acid, 0.400 *M*	35.39	28.1	22.6	37.3
sulfuric acid;	45.51	52.2	65.4	116.4
0.96% water				
$\Delta H^{\pm}$		11.5	19.5 kcal.	21.4 kcal.
$\Delta S^{\pm}$			−39 e.u.	− 8 e.u.
VII in 33.5%	25.15		4.90	3.18
sulfuric acid	35.39		16.3	9.88
	45.51		52.2	31.4
$\Delta H^{\pm}$			21.6 kcal.	21.0 kcal.
$\Delta S^{\pm}$			− 7 e.u.	− 9 e.u.

The correlations of a variety of reactions with the acidity function H_0 in acetic acid solutions serve to support the utility of this function in such a solvent. However, it must not be concluded that questions of detailed mechanism may be decided from such results in non-aqueous solvents. We must regard the conclusions drawn here as tentative.

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(15) D. S. Noyce and W. Reed, THIS JOURNAL, to be published.

(16) R. E. Powell, *J. Phys. Chem.*, **58**, 528 (1954).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE SPRAGUE ELECTRIC CO.]

Solvent Effects in the Reactions of N-Bromosuccinimide with Toluene, Fluorene and Acenaphthene; Evidence for a Polar Mechanism in Propylene Carbonate

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In carbon tetrachloride or benzene, N-bromosuccinimide reacts with toluene, fluorene and acenaphthene to introduce a bromine atom on a methyl group or methylene group adjacent to an aromatic ring. In propylene carbonate, a highly polar solvent, nuclear substituted products are obtained with all three hydrocarbons. When a molar equivalent of boron trifluoride is added, the reaction of fluorene with N-bromosuccinimide in benzene also gives largely the nuclear substituted product, but small amounts of 9-bromofluorene also are formed.

The generally accepted mechanism for the Wohl-Ziegler reaction,[1] in which N-bromosuccinimide is used to introduce a bromine at a carbon atom adjacent to a double bond or an aromatic ring, involves a free radical chain reaction. This mechanism, suggested by Bloomfield,[2] is supported by several facts: (1) The reaction is catalyzed by benzoyl peroxide,[3] azobisisobutyronitrile[4] and cumene hydroperoxide.[4] (2) The reaction is inhibited by hydroquinone, dinitrobenzene, bromanil and iodine.[5] (3) The effects of *m*- and *p*-substituents on the side-chain bromination of toluene[6] are in accord with this mechanism. (4) The observed stereospecificity in brominations of bibenzyl and acenaphthene with N-bromosuccinimide[7] constitutes proof of a two-step mechanism for side-chain bromination and is powerful evidence in support of the Bloomfield suggestion.

Other reactions of N-bromosuccinimide, however, suggest that this reagent may also react by an ionic mechanism involving a heterolytic dissociation of the N–Br bond. Significant among these are the many reported nuclear brominations of aromatic

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(1) (a) A. Wohl, *Ber.*, **52**, 51 (1919); (b) K. Ziegler, A. Spaeth, E. Schaaf, W. Schumann and E. Winkelmann, *Ann.*, **551**, 80 (1942). For more recent review articles see: (c) C. Djerassi, *Chem. Revs.*, **43**, 271 (1948); (d) T. D. Waugh, "N-Bromosuccinimide, Its Reactions and Uses," Arapahoe Chemicals, Inc., Boulder, Colo., May, 1951.

(2) G. F. Bloomfield, *J. Chem. Soc.*, 114 (1944).

(3) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **29**, 573 (1946).

(4) H. J. Dauben, Jr., and E. A. Youngmann, unpublished results. These and additional results by H. J. Dauben, Jr., and L. L. McCoy (*vide infra*) are discussed by C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 382.

(5) H. J. Dauben, Jr., and L. L. McCoy, unpublished results.

(6) E. C. Kooyman, R. Van Helden and A. F. Bickel, *Konikl. Ned. Akad. Wetenschap. Proc.*, **56B**, 75 (1953).

(7) F. D. Greene, W. A. Remers and J. W. Wilson, THIS JOURNAL, **79**, 1416 (1957).