[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MISSOURI]

Action of Ammonia on Esters

BY H. E. FRENCH AND G. G. WRIGHTSMAN[1]

The rate at which amides are formed from esters is affected greatly by variations in structure, and the nature of that effect is of interest. An earlier paper[2] described the behavior of the four butyl acetates toward ammonia. This work has now been extended to cover a number of additional esters of acetic acid, with the work on the butyl esters being repeated because of modifications in procedure from that used in the previous work.

Reagents and Procedure.—The reagent used in this work was prepared by dissolving dry gaseous ammonia in a 50% (by weight) solution of ethyl alcohol in water, and was 6.52 molar with respect to ammonia. This concentration of alcohol was required in order to maintain solution in all cases, further dilution causing the separation of those esters of higher molecular weight. This stock solution was kept at a temperature of 25° by immersion in the thermostat in which the reactions were carried out.

The esters were prepared according to the methods used in the synthesis of the butyl esters in the earlier work. The following boiling points and refractive indices were obtained for these esters: methyl acetate, 56.9–57° 745 mm., 1.3590, 25°; ethyl acetate, 77° 741 mm., 1.3700, 25°; *n*-propyl acetate, 100.5–101.2° 746 mm., 1.3807, 25°; isopropyl acetate, 87.9–88.2° 742 mm., 1.3750, 25°; *n*-butyl acetate, 126.3–126.5° 746 mm., 1.3942, 20°; isobutyl acetate, 116.5–116.7° 746 mm., 1.3901, 25°; *s*-butyl acetate, 111.9–112.1° 742 mm., 1.3865, 25°; *t*-butyl acetate, 97.2–97.5° 746 mm., 1.3840, 20°; *n*-amyl acetate, 146.9–147° 748 mm., 1.4021, 20°; isoamyl acetate, 141° 742 mm., 1.4007, 20°; methyl-*n*-propylcarbinyl acetate, 131.8–132° 746 mm., 1.3960, 20°; diethylcarbinyl acetate, 132.5–133° 748 mm., 1.4005, 20°; benzyl acetate, 140.5–141° 100 mm., 1.5035, 20°.

Six samples of each ester were used. These samples were run into large test-tubes from a pipet calibrated to deliver from 0.0060–0.0065 mole of each of the esters. The samples were then weighed. Ammonia solution was forced from the reservoir in the thermostat into a buret, by means of compressed air, and from 10 to 10.8 cc., depending on the size of the sample, was added to the ester in the test-tubes. These were then sealed off at the constriction and placed in a constant temperature bath maintained at 25°. Each tube contained approximately 10 moles of ammonia and 41 moles of water per mole of the ester. At intervals a sample was removed from the bath, and the reaction stopped by breaking the tip from the tube and washing the contents into a beaker containing 100 cc. of water and 70 cc. of an approximately 1 *N* solution of sulfuric acid. The excess of acid was neutralized at once by the addition of 3 g. of magnesium oxide. The mixture was then distilled from a Kjeldahl flask until the distillate gave no further test for ammonia with litmus. This ammonia represented, in part, excess ammonia in the reaction mixture as well as ammonia from the ammonium acetate formed by hydrolysis of the ester. The ammonia thus distilled from the solution was discarded. The addition of 20 g. of granulated zinc to the mixture eliminated the troublesome bumping which otherwise occurred during the distillation.

Because of the water in the ammoniacal reagent used, hydrolysis and ammonolysis of the esters took place simultaneously. The reaction products were determined in the following manner. Upon completion of the above distillation, the flask contents were cooled and diluted to the original volume, treated with 30 cc. of a 40% solution of potassium hydroxide and again distilled. The ammonia liberated by the hydrolysis of the amide was absorbed in an excess of standard acid, and the amount was determined by back titration. This analytical procedure was tested on samples containing known amounts of recrystallized acetamide, ammonium acetate and acetic acid, and the error in the acetamide determination was found to be less than 0.2%.

The solutions remaining after the second distillation contained potassium acetate, formed in part by hydrolysis of the ester during the reaction and in part from the hydrolysis of the amide, as well as magnesium and potassium sulfates and hydroxides. These mixtures were analyzed for acetic acid by the method of Mudgen and Wimmer.[3] The method consists in the fusion of the potassium salt with potassium hydroxide and cupric oxide, and titration of the resulting oxalic acid with permanganate. Blank determinations on mixtures of comparable composition to those obtained in these reactions showed that from ten to twelve hours of fusion were required to give complete conversion of the acetic acid. A maximum error of 0.3% was obtained for a series of such blank determinations involving various quantities of acetic acid. This total acetic acid minus an amount equivalent to the acetamide represented the acetic acid obtained by the hydrolysis of the ester during the reaction. A summary of the results is given in the tables.

Our principal interest in the present work was the formation of the amide as affected by variations in the structure of the alcohol radical of the ester. The extent of hydrolysis, however, was considerable, amounting, with esters of primary alcohols, to as high as 16% of the total reaction, and increasing in importance with esters of secondary and tertiary alcohols, where it accounted for as high as over 50% of the total reaction products. Both reactions varied in the same direction as the structures were altered.

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[1] This paper is an abstract of the thesis submitted by Mr. Wrightsman to the graduate faculty of the University of Missouri.

[2] French, Johnson and Ratekin, THIS JOURNAL, **58**, 1346 (1936).

[3] Mudgen and Wimmer, *Z. angew. Chem.*, **46**, 117 (1933).

TABLE I

TOTAL PERCENTAGE REACTION IN

Acetate	5	10	15	20	30	40	50	80	100	130	160	180	200	260	320	400	480	500	600 hrs.
Methyl	62	78		90	93		94												
Benzyl	44	62	73																
Ethyl	21	35		57	72			95	97										
n-Propyl					52			85	89	94			97						
n-Butyl				34			67	82	87		96								
n-Amyl				28	39				78		86								
Isobutyl					41			69	76	83		92							
Isoamyl				27					72		80		85						
Isopropyl				14		23			44			64	67	77					
s-Butyl				5				21				40	44		56				64
Methyl-*n*-propylcarbinyl									23		34		38		48	54		60	
Diethylcarbinyl											23		26		34	40	46	47	
t-Butyl													5					9	10

TABLE II

COURSE OF THE REACTION AT 25°

Acetate	Hours	% Reaction	% Ammonolysis	% Hydrolysis
Methyl	20	90	82	8
Benzyl	15	73	62	11
Ethyl	100	97	81	16
n-Propyl	100	89	75	14
n-Butyl	100	87	72	15
n-Amyl	100	78	67	11
Isobutyl	100	76	61	15
Isoamyl	100	72	62	10
Isopropyl	100	44	27	17
	200	67	45	22
s-Butyl	200	44	26	18
Methyl-*n*-propylcarbinyl	100	23	11	12
	200	38	19	19
Diethylcarbinyl	200	26	12	14
t-Butyl	200	5	2	3

The reaction with ammonia took place readily with esters of primary alcohols. With those of normal alcohols there was a continual decrease in the velocity of the reaction as the molecular weight increased. The presence of side chains in the alcohol radical decreased the speed of reaction, an effect which increased in importance as the side chain approached the oxygen atom. Comparison of the extent of reaction at one hundred hours for the normal and isoamyl, and methyl-*n*-propylcarbinyl acetates shows an appreciable effect for a methyl group three carbons removed from the oxygen, with a very rapid falling off of reaction rate as the methyl group approaches the oxygen. The behavior of the normal and isobutyl esters and the two propyl esters is in accord with this. It is of interest also that the reactivity of the ester of diethylcarbinol is less than that of the isomeric ester of methyl-*n*-propylcarbinol.

The decreasing activity of esters as the alcohol radical is varied from primary to secondary to tertiary is found in both hydrolysis and ammonolysis reactions, and is in direct contrast to their behavior toward anhydrous hydrogen bromide (which splits the ester at the ether linkage) and to the behavior of ethers. Here the tertiary radical is removed much more readily than the secondary which is much more easily removed than the primary.[4]

Summary

1. The action of an aqueous–alcoholic solution of ammonia on a number of esters of acetic acid has been investigated.

2. Reactivity decreases with increase in the molecular weight, with introduction of side chains in the alcohol radical, and with the nearness of the side chains to the oxygen atom. Esters of primary alcohols react readily, those of secondary alcohols much more slowly, and tertiary butyl acetate extremely slowly.

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[4] Tronov and Ladigina, *Ber.*, **62B**, 2844, 2850 (1929).