

ART. XXXIX.—*The Preparation of Acetamide by the Action of Ammonium Hydroxide and Ethyl Acetate*; by I. K. and M. A. PHELPS.

[Contributions from the Kent Chemical Laboratory of Yale Univ.—clxv.]

It has been stated by Hofmann* that the action of aqueous ammonia upon ethyl acetate at ordinary temperatures yields after several days' standing considerable amounts of acetamide, but that the amount of acetamide by no means corresponds to the amount of ethyl acetate taken. Hofmann further states that according to a communication from Dr. Bannow the yield of acetamide, even when formed in large quantities, is usually not much above 70 per cent of that theoretically demanded. In this same communication Hofmann makes a similar statement in regard to the action of ethyl formate.

In a former paper from this laboratory† conditions have been shown under which very nearly the theoretical yield of formamide by the action of ammonium hydroxide and ethyl formate is obtained. Now it has been found that conditions closely similar will give theoretical yield as well in the case of ethyl acetate and aqueous ammonia.

For the work given here ethyl acetate of commerce was treated in a separating funnel with sodium carbonate solution, and, after separating from this, was washed with distilled water. The ethyl acetate thus purified from acid impurities was separated as completely as possible from the water, dried over fused calcium chloride and then treated again with a fresh portion of fused calcium chloride before fractioning. Portions boiling between 77° and $77^{\circ}.2$ were taken as pure ethyl acetate.

Definite portions of the pure ethyl acetate were weighed, and, after chilling below zero in an ice and salt mixture, were mixed in a stoppered reagent bottle with definite volumes of ammonium hydroxide. In some of these experiments the ammonium hydroxide was the pure concentrated ammonium hydroxide of commerce; in others the ammonium hydroxide was made more concentrated by saturating at -10° the pure concentrated ammonium hydroxide of commerce with dry ammonia gas obtained by heating concentrated ammonium hydroxide in a flask connected with a return condenser and drying further the ammonia by passing it through a lime tower; while in a third series of experiments the product obtained by mixing in the cold in a stoppered reagent bottle the ethyl acetate and ammonium hydroxide was saturated in the cold with dry ammonia gas obtained in the manner given

* *Berichte*, xv, 977.

† *This Journal*, xxiv, 173.

above. In every case, after the solution had stood a sufficient time in the reagent bottle stoppered tightly so that the ammonia gas should not escape, it was transferred to a 250^{cm}³ distilling flask, connected with a 100^{cm}³ distilling flask in the usual way for a vacuum distillation, with the use of the least amount of absolute alcohol to rinse the sides of the bottle. The low boiling impurities, ammonia, alcohol, and water, were removed by fractioning in vacuo in the usual way, the 250^{cm}³ flask being heated in a bath of hot water finally at 60° for fifteen minutes after the pressure on the manometer registered 15^{mm}. The acetamide left in the flask was distilled by heating the flask in an acid potassium sulphate bath at 140° to 150°, and was collected in the receiver, cooled by a stream of cold water, and weighed.

The experiments of section A are those in which the pure ammonium hydroxide of commerce was used with the ethyl acetate, and after standing suitably the mixtures were distilled in vacuo as given above.

The experiments of section B were conducted in the same way as those in section A, except that the ammonium hydroxide used was saturated at -10° with dry ammonia before mixing in the cold with the ethyl acetate.

The experiments of section C were conducted in the same way as those of A excepting that the entire mass of ethyl acetate and ammonium hydroxide after mixing in the cold was saturated with dry ammonia gas at -8° to -10°.

From an inspection of the results recorded in section A it is seen that the volume of ammonium hydroxide taken for a given weight of ethyl acetate, as well as the time allowed for the interaction of the ethyl acetate and ammonia, influences the yield of acetamide. The theoretical yield can be obtained with the proportion and concentration of the reagents used here only on long standing. Two weeks' standing at ordinary temperatures with so large an amount as 75^{cm}³ of the ammonium hydroxide for 50 gm. of ethyl acetate will give the yield required by theory, although for smaller proportions of the ammonium hydroxide that time is not sufficient.

It is evident from the results given in section B that a solution of saturated aqueous ammonia tends to give a larger yield of acetamide in a given time than can be obtained by weaker aqueous ammonia.

In section C the results show that in shorter time than by the procedure in experiments given in A and B of the table the theoretical yield of acetamide may be obtained by saturating in the cold the mixture of ethyl acetate and ammonium hydroxide and allowing it to stand either four or six days according to the proportion of the aqueous ammonia present.

TABLE I.

A						Acetamide	
Treatment with NH ₄ OH.						Theory	Found
No.	Ethyl acetate gram.	Ammonium hydroxide		Reaction time		gram.	gram.
		cm ³	Sp. g.	Days	Hrs.		
(1)	50	50	0.90	3	22	33.57	21.70
(2)	50	50	0.90	6	19	33.57	25.60
(3)	50	50	0.90	13	--	33.57	29.00
(4)	45.4	50	0.90	126	--	30.80	30.36
(5)	50	75	0.90	3	23	33.57	26.89
(6)	50	75	0.90	6	--	33.57	30.15
(7)	50	75	0.90	8	--	33.57	31.18
(8)	50	75	0.90	13	--	33.57	34.10
B							
Treatment with NH ₄ OH saturated with NH ₃ .							
(9)	50	50	---	3	19	33.57	21.03
(10)	50	50	---	12	--	33.57	32.80
(11)	50	50	---	49	--	33.57	33.12
(12)	50	78	---	3	22	33.57	28.81
(13)	50	78	---	6	22	33.57	32.53
C							
Treatment with NH ₄ OH and saturation of the mixture with NH ₃ .							
(14)	50	50	0.90	3	16	33.57	25.78
(15)	50	50	0.90	6	--	33.57	33.71
(16)	50	50	0.90	12	6	33.57	33.82
(17)	50	50	0.90	20	--	33.57	33.47
(18)	50	75	0.90	--	23	33.57	17.72
(19)	50	75	0.90	2	--	33.57	30.08
(20)	50	75	0.90	3	--	33.57	31.63
(21)	50	75	0.90	4	--	33.57	33.62
(22)	50	75	0.90	4	6	33.57	34.00

It is evident that the time of completion of the reaction is dependent upon the concentration of the ammonia.

It was found that the mixture of ammonium hydroxide and ethyl acetate became homogeneous in the experiments of section A in about three days, in B in somewhat less time, and twenty-four hours in C. In experiment (18) the mass became homogeneous at the end of twenty-three hours, and in this single instance distillation was made as soon as this phenomenon appeared. It is evident that the formation of acetamide progresses slowly and is not at an end as soon as the mass becomes homogeneous.

It was found by experiment that a known weight of pure acetamide treated with 10^{cm}³ of water and fractioned in vacuo

could be recovered with a loss of less than 0.05 gm. The acetamide tends to hold traces of water; and it was not found possible to remove it by fractional distillation in vacuo without danger of loss of very small amounts of acetamide.

The presence and amount of ammonium salt in the acetamide obtained in the procedure outlined above were tested for by the use of a solution of sodium cobalti-nitrite. An experiment showed that 0.0002 gm. of ammonium chloride could be readily detected in the presence of 0.50 gram of acetamide. The acetamide obtained directly by fractioning in vacuo, as given above, was found to contain traces of ammonia and ammonium salt. In experiment (8) the crude material was transferred after weighing the product obtained from the vacuum distillation to a watchglass and allowed to stand in a desiccator over sulphuric acid for twenty-four hours, and the loss sustained was 0.62 gm., presumably largely water with some ammonia. Some of this loss must have been acetamide also, for by a separate experiment with pure acetamide recrystallized from benzene it was found that acetamide continually lost in weight in a sulphuric acid desiccator. The acetamide from experiment (8) after being dried showed the presence of not more than 0.30 gm. of ammonium salt, estimated by the amount of precipitate produced with sodium cobalti-nitrite as compared with the amount of precipitate obtained under similar conditions with ammonium chloride, pure acetamide and sodium cobalti-nitrite. The material obtained in experiment (22) was redistilled with an air condenser under ordinary atmospheric pressure and yielded 27.5 gm. of product boiling between 221° and 222°. This product showed on testing with sodium cobalti-nitrite no ammonium salt. Theoretically, more ammonium salt might be present in those cases where the standing is longest. But it was found on redistillation, under ordinary atmospheric conditions, of the acetamide obtained directly by the processes given above, that ammonium salt was not present in sufficiently large amounts in the different experiments to be noticeable.

It is clear from the work given that acetamide with only traces of impurity may be obtained in quantities barely less than quantitative for the amount of ethyl acetate taken, if ethyl acetate and ammonium hydroxide are mixed in the cold and allowed to stand a suitable length of time. Increasing the amount of ammonium hydroxide employed shortens the time of standing necessary for a theoretical yield, and increasing the concentration of ammonia by saturating the mixture of ethyl acetate and ammonium hydroxide in these proportions with ammonia gas further diminishes, by one-half or more, the time of standing.