

The Heats of Aminolysis of *n*-Butyl Thiolacetate and Acetic Anhydride

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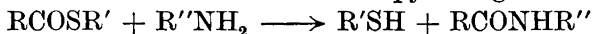
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The heat of aminolysis of *n*-butyl thiolacetate by *n*-butylamine was determined at 25°C. For the idealized, isothermal aminolysis reaction

$n\text{-BuSAc (l)} + n\text{-BuNH}_2 \text{ (l)} \rightarrow n\text{-BuSH (l)} + n\text{-BuNHAc (l)}$
the enthalpy change was found to be -13.7 ± 0.2 kcal/mole. The heat of aminolysis of acetic anhydride was also determined and from the obtained value and known values of the heats of hydrolysis of acetic anhydride and *n*-butyl thiolacetate a value of -13.80 ± 0.15 kcal/mole was derived for the heat of aminolysis of *n*-butyl thiolacetate.

The heat of hydrolysis of *n*-butyl acetamide was calculated to be 12.69 ± 0.10 kcal/mole.

Recently much interest has been directed towards S-acyl compounds as acetylating agents in biochemical systems. It is known that a thiolester of an amino acid easily forms a peptide by aminolysis¹. In connection with previous work² on energy relationships of S-acylated compounds it seemed of interest to determine the enthalpy change of the reaction



The reaction can be looked upon as an model for peptide formation, where RCOSR' corresponds to a S-acyl activated amino acid and R''NH₂ to an amino acid.

In the simplified system investigated here, R was methyl and R', R'' were *n*-butyl. Thus the thiol ester was *n*-BuSAc and the amine was *n*-BuNH₂. However, the value obtained might be significantly in error. It was therefore checked by an indirect determination, by measuring the heat of aminolysis of acetic anhydride and combining this with known values for the heats of hydrolysis of Ac₂O and *n*-BuSAc, from which the heat of aminolysis of *n*-BuSAc could then be calculated.

PART I. AMINOLYSIS OF *n*-BUTYL THIOLACETATE

Experimental

Materials. *n*-BuSAc was prepared and purified according to Ref.³ The equivalent weight was determined by iodometric titration of the thiol formed by alkaline hydrolysis³.

The equivalent weight indicated 100.0 % purity. $n_D^{25} = 1.4584$, $d_4^{25} = 0.9385$. n -BuNH₂ (purum grade) was dried by refluxing with NaOH-pellets. The amine was distilled through an efficient column and a fraction boiling at 76.2°C (760 mm Hg) was collected. Potentiometric titration gave an equivalent weight corresponding to 99.6 % purity.

Auxiliary substances. n -BuSH was freshly distilled and its purity as checked by iodometric titration was found to be 100.0 %. n -BuNHAc was prepared from n -BuSAc and n -BuNH₂. The synthesis and physical data of the substance are described below.

Chemistry of the process. In order to secure a rapid reaction and to avoid side reactions the aminolysis was carried out in butyl amine. However, the thiol formed was extremely rapidly oxidised by air in the alkaline medium. The rate of oxidation was studied by exposing to air solutions of n -BuSH in n -BuNH₂. After a given time the solution (5 ml of a 3 % solution in a 100 ml conical flask) was cooled with dry ice, acidified with glacial acetic acid and titrated with iodine. The experiments showed that ca. 10 % of the thiol was oxidised within 30 min.

In order to check that the reaction products of the aminolysis reaction were as expected, the following synthesis was carried out. 20.0 g of n -BuSAc were added rapidly to 150 ml of n -BuNH₂. After 30 min at room temperature the excess of amine and the thiol formed were driven off by distillation at atmospheric pressure. The presence of thiol in the distillate was confirmed by the nitroprusside reaction. The remaining product was distilled at reduced pressure. n -BuNHAc was collected at 140–141°C and 21 mm Hg. Yield 16.6 g or 95 %. After further distillation the physical data of the substance were in good agreement with those given in the literature³. B. p. 230°C at 760 mm Hg, $n_D^{25} = 1.4391$, $d_4^{25} = 0.8951$.

Apparatus. The reactions were carried out in an isothermal calorimeter which will be described in a forthcoming paper⁴.

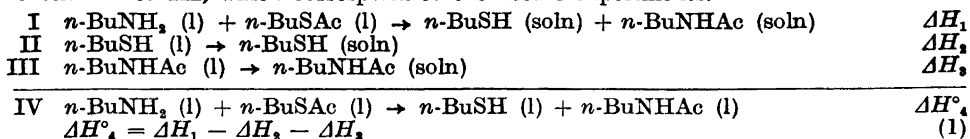
Calibration. The heat capacity of the system was determined electrically by passing a known current for a known time (20 min) through the heating element. Thermal leakage was calculated by the Regnault-Pfaundler's method. The calibration experiments was carried out after the aminolysis experiments. In the runs, corrections were made for the small differences in heat capacity of the ampoule and its content.

Procedure. As stated above, it was not possible to avoid air oxidation of the thiol formed during an experiment. In order to suppress the influence of this exothermic reaction a small amount of butanethiol was added to the solution prior to the reaction. The heat of oxidation increased much less than expected from the increase in thiol concentration due to aminolysis. However, a significant error was introduced, which could be seen from the values of the thermal leakage constant, K . If thiol was added prior to the reaction the value of K was only 10 % lower than in calibration experiments whereas the value of K was found to be negative when butanethiol was not added.

The calorimeter was charged with 90 ml of n -BuNH₂ to which 9 mmoles of n -BuSH were added. The sealed glass ampoule contained ca. 3 mmoles of n -BuSAc. After equilibration the reaction was started by breaking the ampoule. The duration of the reaction period was 45 min, so that the thermal leakage had to be calculated by the Regnault-Pfaundler method. As the K -values obtained from the runs were abnormally low, the mean of those from the calibration experiments was used in the calculations. The small systematic error introduced by the oxidation of the thiol formed during the aminolysis cancels out to a great extent by the error in the heat of solution experiment of butanethiol — the only difference between the two series of experiments being the slow appearance of thiol in the aminolysis and the momentary mixing of thiol and solvent in the solution experiment.

Heat of solution measurements. n -BuSH: In order to obtain a close similarity between the solution measurements and the aminolysis experiments, the reaction period was kept at 45 min. n -BuNHAc: The reaction period was 5 min and R_i and R_f were obtained graphically.

Corrections to standard state. The idealised aminolysis reaction IV is obtained from reactions I to III, which correspond to the actual experiments.



Units of measurement. The results of the calorimetric experiments are expressed in terms of the defined calorie equal to 4.1840 abs. joules and refer to the isothermal process at 25°C and to the true mass. The molecular weights were computed from the 1951 Table of international atomic weights⁶.

Results

The experimental results are summarised in Tables 1 to 3. In Table 1 the results from the calibration experiments are given. The first column shows the input of electrical energy, the second the expression proportional to the temperature increase and the third the value of the heat capacity in calories per unit of $\log (R_i/R_t)$. Uncertainties are given as the standard deviation of the mean.

Table 1. Calibration experiments.

q , cal	$10^4 \times \log (R_i/R_t)$	$10^{-2} \times \epsilon$
36.34	103.69	35.05
36.43	104.09	35.00
36.66	104.35	35.13
36.56	104.39	35.02
	Mean	35.05 ± 0.03

Tables 2 and 3 give the results of the aminolysis experiments. The first column gives the amount of substance, the third the amount of heat evolved, and the last gives the enthalpy change in kcal/mole.

Table 2. Determination of the heat of aminolysis of *n*-butyl thioacetate by *n*-butylamine.

mmole	$10^4 \times \log (R_i/R_t)$	q , cal	$-\Delta H$, kcal/mole
3.034	131.20	45.99	15.16
2.823	121.01	42.41	15.02
2.864	122.72	43.01	15.02
3.080	133.27	46.71	15.17
2.919	126.61	44.38	15.20
	Mean		15.11 ± 0.04

Table 3. Heat of solution measurements.

Substance	mmole	$10^4 \times \log (R_i/R_t)$	q , cal	$-\Delta H$, kcal/mole
<i>n</i> -BuSH	2.915	1.02	0.36	0.12
	2.778	-1.77	-0.62	-0.22
	3.112	0.11	0.04	0.01
	3.429	-0.56	-0.20	-0.06
	Mean			-0.04 ± 0.07
<i>n</i> -BuNHAc	3.077	12.12	4.25	1.38
	3.105	13.05	4.57	1.47
	Mean			1.42 ± 0.04

From eqn. (1) ΔH_4^0 is calculated to be 13.73 ± 0.09 kcal/mole. However, uncertainty in the K -value used is estimated to be 2 %. This will cause an uncertainty in ΔH_4 amounting to 0.1 kcal/mole. Therefore, the best value that can be obtained from these experiments is believed to be

$$\Delta H_4^0 = -13.7 \pm 0.2 \text{ kcal/mole.}$$

PART II. AMINOLYSIS OF ACETIC ANHYDRIDE

Materials. Ac_2O was freshly distilled immediately before the experiments. Its equivalent weight (determined by potentiometric titration of the acetic acid formed by hydrolysis) indicated 99.9 % purity. $n\text{-BuNH}_2$ was treated as given in part I.

Auxiliary substances. HOAc was purified by freezing out 4 times. The equivalent weight corresponded to 100.0 % purity. $n\text{-BuNHAc}$ was prepared from Ac_2O and $n\text{-BuNH}_2$. Details of the method of synthesis and physical data of the substance are given below. Benzene, free from thiophene was dried with KOH -pellets and distilled.

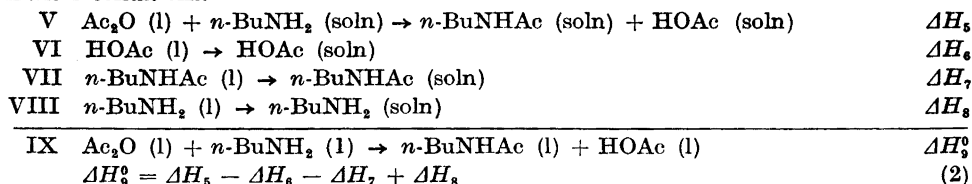
Chemistry of the process. Ac_2O reacts vigorously with pure $n\text{-BuNH}_2$. In the calorimetric experiments the reaction rate was moderated by performing the aminolysis in benzene solution. The reaction products were soluble in this medium at the concentrations used. To confirm that $n\text{-BuNHAc}$ was obtained in the reaction, the following experiment was carried out.

0.3 mole of Ac_2O was added rapidly to a solution of 1.2 moles of $n\text{-BuNH}_2$ in 150 ml benzene. The temperature of the mixture was kept below 30°C by cooling with ice water. After ca. 10 min the benzene and the excess of amine was distilled off. To the residue, 50 ml of water were added and the solution was extracted three times with ether. The product was dried with anhydrous CaCl_2 and the ether distilled off. The residue was distilled under reduced pressure through an efficient column. 28.6 g (83 %) $n\text{-BuNHAc}$ was collected at 92.5°C (1 mm Hg). The physical data of the substance were in good agreement with those given in the literature³. B.p. 230°C at 760 mm Hg, $n_D^{25} = 1.4393$, $d_4^{25} = 0.8950$.

Apparatus. See Part I.

Calibration experiments. The calorimeter was calibrated as in Part I, except that the heat was supplied for 4 min only. The main period lasted for 7 min and R_i and R_f were obtained graphically.

Correction to standard state. The idealized aminolysis reaction IX is obtained from reactions V to VIII which correspond to the reactions taken place under actual experimental conditions.



The experimental results are summarized in Tables 4 to 6.

Table 4. Calibration experiments.

q cal	$10^4 \times \log (R_i/R_f)$	$10^{-3} \times \epsilon$
35.62	123.35	28.88
35.49	121.02	29.32
35.10	120.94	29.02
35.58	123.42	28.83
35.43	121.71	29.11
32.62	112.64	28.96
	Mean	29.02 ± 0.08

Table 5. Heat of aminolysis of acetic anhydride by *n*-butylamine.

mmole	$10^4 \times \log (R_i/R_f)$	<i>q</i> cal	$-\Delta H$, kcal/mole
1.073	144.13	41.83	38.98
0.983	132.57	38.47	39.14
1.102	148.43	43.07	39.08
1.038	140.18	40.68	39.19
1.207	163.38	47.41	39.28
		Mean	39.13 \pm 0.06

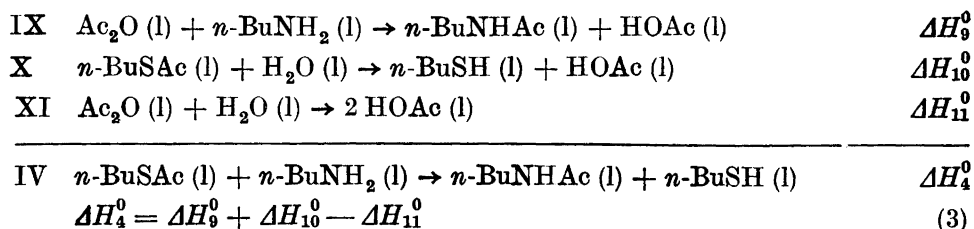
Table 6. Heat of solution measurements.

Substance	mmole	$10^4 \times \log (R_f/R_i)$	<i>q</i> , cal	$-\Delta H$, kcal/mole
HOAc	1.389	64.77	18.79	13.53
	1.376	64.11	18.60	13.52
	1.041	48.25	14.00	13.45
			Mean	13.50 \pm 0.02
<i>n</i> -BuNHAc	1.202	-6.40	-1.86	-1.55
	1.115	-5.82	-1.69	-1.52
	1.027	-5.62	-1.63	-1.59
			Mean	-1.55 \pm 0.04
<i>n</i> -BuNH ₂	0.827	-1.46	-0.42	-0.51
	0.710	-1.21	-0.35	-0.49
	1.073	-2.13	-0.62	-0.58
			Mean	-0.53 \pm 0.03

From eqn. (2) is obtained $\Delta H_9^0 = -26.65 \pm 0.08$ kcal/mole.

Calculation of the heat of aminolysis of *n*-BuSAc

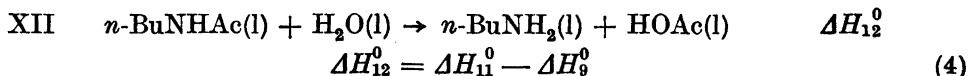
The heat of aminolysis of *n*-BuSAc (reaction IV) can be obtained from ΔH_9^0 and the known heats of hydrolysis of *n*-BuSAc² and Ac₂O⁶, ΔH^0 equals -1.09 ± 0.06 kcal/mole and -13.92 ± 0.05 * kcal/mole, respectively.



Thus we find ΔH_4^0 to be -13.82 ± 0.11 kcal/mole. This value is in good agreement with the value given in Part I. Taken into consideration the more favourable experimental conditions of the indirect determination $\Delta H_4^0 = -13.80 \pm 0.15$ kcal/mole seems at present to be the best value that can be given.

Calculation of the heat of hydrolysis of *n*-BuNHAc

It is well known that N-alkyl acetamides do not easily hydrolyze at room temperature. It is therefore difficult to obtain a good value for the heat of hydrolysis from direct measurements. However, by subtracting reaction IX from reaction XI we get the idealized hydrolysis reaction XII



Thus the heat of hydrolysis of *n*-BuNHAc is calculated to be 12.73 ± 0.10 kcal/mole.

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* The value has been recalculated to 25°C. The uncertainty is an estimate.

Received January 24, 1958.