ACTION OF LIQUID AMMONIA UPON ACETONE-COMPOUNDS OF α-HYDROXY-ACIDS[1].

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In a previous communication[2] it was reported that acetone-compounds of α-hydroxy-acids were hydrogenated into α-glycols in the presence of a catalyzer generally used in reducing esters into alcohols. In the present communication it will be reported that the acetone-compounds react with ammonia similarly as esters do, giving rise to acid amides.

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(1) Studies on Hydroxy-acids and their Derivatives. IV.
(2) This Bulletin, **10** (1935), 531.

The general method for the preparation of acid amides from esters is to pass gaseous ammonia into alcoholic solutions of esters. This method is unfavourable for the present compounds owing to their small solubilities in cold alcohol. The procedure adopted here consists in keeping the acetone-compounds in contact with an excess of liquid ammonia, reaction temperature being varied to find out the best condition for producing acid amides.

In all experiments at elevated temperature (100°) for shorter duration and at room temperature for longer duration it was found that acid amides were readily formed and the following four compounds were prepared from corresponding acetone-compounds.

Amide of *dl*-lactic acid	$CH_3 \cdot CHOH \cdot CONH_2$	m.p. 78.5–79.0°
Amide of *l*-leucic acid	$(CH_3)_2CH \cdot CH_2 \cdot CHOH\ CONH_2$	m.p. 84–85°
Amide of *dl*-mandelic acid	$C_6H_5 \cdot CHOH \cdot CONH_2$	m.p. 133–134°
Amide of *l*-phenyl-lactic acid	$C_6H_5 \cdot CH_2 \cdot CHOH \cdot CONH_2$	m.p. 112.5–113.5°

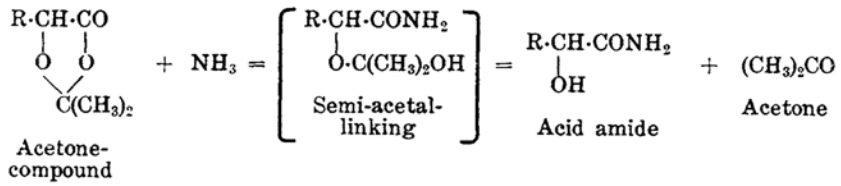
In all cases, the yield in the reaction at room temperature is better than that at elevated temperature and the samples obtained at both conditions are always contaminated with a considerable amount of deeply coloured tarry matter.

Recently Glattfeld and Macmillan[3] pointed out the fact that an inequality of reactivity towards ammonia exists between various types of lactones, namely, at the boiling point of liquid ammonia under ordinary pressure, lactones of sugar acid type yielded acid amides, while other lactones such as γ-butyro-lactone failed. At the same condition of temperature, an attempt to obtain acid amides from acetone-compounds was tried.

In the reaction at lower temperature for shorter duration, the procedure was essentially to dissolve the acetone-compound in liquid ammonia kept in a Dewar vessel and to allow the solution to stand overnight. During the reaction ammonia freely evaporated and the temperature in the reaction vessel settled nearly down to −33°, the boiling point of liquid ammonia under ordinary pressure. The amides obtained in these cases were most satisfactory both in purity and in yield (amounting to 85-95%). The same procedure was again tried with ethyl esters of two of these hydroxy-acids. From these esters, amides obtained were but in poor yields (2 and 25%) and larger parts of esters were recovered unattacked. It can be said that here too an inequality of reactivity was observed and acetone-compounds of α-hydroxy-acids are far more reactive to ammonia than the corresponding esters.

The reaction mentioned above can be expressed as the formation of acid amides along with regeneration of acetone:

(3) *J. Am. Chem. Soc.*, **56** (1934), 2481.



Besides the main products, diacetonamine $(CH_3)_2C(NH_2)\cdot CH_2\cdot CO\cdot CH_3$, formed by the reaction of ammonia with acetone, was identified.

Experimental Part.

The acetone-compounds were prepared from hydroxy-acids and acetone by dehydration with conc. sulphuric acid[4]. They have the following constants:

Acetone-*dl*-lactic acid	b.p. 58–59° under 18 mm.
Acetone-*l*-leucic acid	b.p. 85–86° under 14 mm.
Acetone-*dl*-mandelic acid	m.p. 46–47°
Acetone-*l*-phenyl-lactic acid	m.p. 63–64°
Ethyl *dl*-lactate (Takeda)	b.p. 58° under 19 mm.
Ethyl *dl*-mandelate[5]	b.p. 132–133° under 13 mm.

I. **Reaction at Elevated Temperature.** Twenty to twenty-five grams of acetone-compounds (0.10–0.15 mol) and 20–25 c.c. of dry liquid ammonia (representing 6–7 mols of ammonia to 1 mol of acetone-compound) were put into an autoclave (capacity 250 c.c.), kept below −35° by cooling with solid carbon dioxide and acetone. After closing, the autoclave was maintained at 100° for five hours by immersing it into boiling water.

II. **Reaction at Room Temperature.** Acetone compound and ammonia (just in the same amount and the same ratio as above) were put into an autoclave (300 c.c.), which was allowed to stand for two weeks at room temperature.

III. **Reaction at Lower Temperature.** Five to six grams of acetone compounds or esters (0.03–0.04 mol) together with 25–30 c.c. of liquid ammonia (25–30 mols to 1 mol of acetone-compound or ester) were put into a silvered Dewar vessel (capacity 100 c.c.) provided with soda-lime tube and allowed to stand overnight. Though the acetone-compounds seem to be fairly soluble in liquid ammonia, it was necessary to use such a large excess of ammonia so as to cover the whole mass of solid acetone-compound with the liquid.

After the lapse of time mentioned above, the gas-outlet of the autoclave was opened and the remaining ammonia was freely evaporated. The contents of the vessel were in a state of viscous liquid (mandelamide was found as crystalline cake), which were poured into an open dish placed on a water bath. By blowing over the surface of the liquid the evaporation of ammonia was quickened. In general, the amide crystallized as soon as the ammonia was completely removed. The vessels here used were all rinsed with hot alcohol, and the small amount of the amide obtained from the washings was combined with the main crop.

(4) H. Ôeda, this Bulletin, **10** (1935), 187.
(5) Prepared from *dl*-mandelic acid (Merck) and ethyl alcohol by dehydration with conc. sulphuric acid.

The crude amide thus separated was washed with a definite amount of benzene (when cold, it does not dissolve the amide) to remove the tarry matter. The solvent and a little moisture[6] adhering the amides were completely removed in vacuum. The yields of crude amides[7] and the analytical results of recrystallized samples are shown in Tables 1 and 2.

Table 1.

Starting material	Acetone-compound			Ester
Reaction temperature	100°	room temp.	ca. -33°	ca. -33°
Lactamide	47%	—	85%	less than 2.5%
Leucic acid amide	49%	79%	90%	—
Mandelamide	70%	92%	95%	25%
Phenyl-lactamide	55%	88%	90%	—

Table 2.

Substance	Solvent of recrystallisation	Analytical results	
		Found	Calculated
Amide of *dl*-lactic acid[8] m.p. 78.5–79°.0 (corr.)	benzene-alcohol (3 : 1)	N, 15.76	C_3H_7ON : N, 15.74%
Amide of *l*-leucic acid[9] m.p. 84–85° (corr.)	benzene-alcohol (10 : 1)	N, 10.77	$C_6H_{13}ON$: N, 10.69%
Amide of *dl*-mandelic acid[10] m.p. 133–134° (corr.)	absolute alcohol	N, 9.34	C_8H_9ON : N, 9.27%
Amide of *l*-phenyl-lactic acid[11] m.p. 112.5–113.5° (corr.)	benzene-alcohol (2 : 1)	N, 8.46	$C_9H_{11}ON$: N, 8.48%
Acid oxalate of diacetonamine[12] m.p. 124–125° (corr.) (hydrate)	95% alcohol	N, 6.49 H_2O, 8.22	$C_6H_{13}ON \cdot C_2H_2O_4 \cdot H_2O$: N, 6.27% H_2O, 8.07%

(6) During evaporation of ammonia, owing to considerable cooling condensation of water was unavoidable.

(7) The reaction at lower temperature was tried in a smaller scale corresponding to a quarter of the other reactions. Hence the yields in these experiments are shown by numbers rounded up to every 5 mol %. (Accuracy of weighing was 0.1 g. It corresponds to 2–3 mol % in yields of amides.)

(8) M.p. 74° given by Wislicenus, *Ann.*, **133** (1865), 261.

(9) Amide of active acid is unknown. That of *dl*-acid melts at 51–52°, Nicolle, *Bull. soc. chim.*, [4], **39** (1926), 60.

(10) The same m.p. is given by McKenzie and Wren, *J. Chem. Soc.*, **93** (1908), 311.

(11) M.p. 112–113° given by McKenzie, Martin, and Rule, *ibid.*, **105** (1914), 1588.

(12) M.p. 126–127° given by Everest, *ibid.*, **115** (1919), 591.

In every case, unreacted acetone-compound was never obtained, while in the experiments with esters, 4.1 g. out of 5.3 g. of ethyl lactate and 4.3 g. out of 7.2 g. of ethyl mandelate were recovered from the reaction products by vacuum distillation and amides were isolated from the residue of distillation.

The combined benzene solution obtained from four sets of experiments with acetone-compounds at lower temperature was evaporated to a small bulk, to which a saturated solution of oxalic acid in 95% alcohol was added. The whole mass turned to a crystalline oxalate and it was collected by suction. The oxalate obtained was extracted with a large bulk of boiling 95% alcohol. The unextracted portion was found to be ammonium oxalate by converting it into platinic double chloride (Found: Pt, 43.85. Calc. for $(NH_4)_2PtCl_6$: 43.94%). The diluted alcoholic extract was cooled and a little ammonium oxalate again precipitated. After filtration the solution was evaporated to a small bulk, from which an oxalate was isolated. It was found to be acid oxalate of diacetonamine (Table 2).

The tarry matter obtained from the reactions at higher and room temperatures gave also oxalates. But, after removal of the oxalates, there remained a considerable amount of resin, that means the tar comprised a part which did not form oxalate. It did not distil in acidic nor alkaline state even in vacuum, no further study of this resin has been made.

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