was then cooled to 10°, when a small amount of precipitate formed. This was filtered off and crystallized from alcohol. M. p. 121°. The filtrate was evaporated to dryness on the water bath and the residue taken up in hot absolute alcohol. On cooling the alcoholic solution, flaky crystals of isobutylacetamide formed. This process was repeated several times. The crystals melted at 121°, with a slight sublimation at 118.5°. The recorded[1] m. p. is 120°. The yield was about 70% of the theory.

Calc. for $(CH_3)_2CH(CH_2)_2CONH_2$: 12.17%. Found: 12.22% N.

Conclusions.

1. We have thus prepared 9 amides in the pure condition from the corresponding nitriles. Their analyses (for nitrogen) have been made and some of their properties studied.
2. We have found that some of the nitriles, which formerly could not be transformed into amides by the ordinary concentration of hydrogen peroxide, can be transformed by more concentrated solutions of the peroxide.
3. It has been shown that the change of nitriles into corresponding amides by hydrogen peroxide, under stated conditions, is a generally applicable method.

St. Louis, Mo.

[Contribution from the Otho S. A. Sprague Memorial Institute, Laboratory of Clinical Research, Rush Medical College.]

THE PREPARATION OF GLYCOLLIC ACID.

By Edgar J. Witzemann.

Received November 1, 1916.

Perhaps the simplest and most inexpensive method of obtaining glycollic acid hitherto has been the method of Hölzer[2] in which monochloroacetic acid is boiled in aqueous solution with somewhat more than the calculated quantity of calcium carbonate until no more goes into solution. The solution is then filtered and allowed to cool and crystallize. The crystals of calcium glycollate ($Ca(C_2H_3O_2)_2.4H_2O$) are washed until free from calcium chloride. Sometimes a double salt of calcium chloride and glycollate separates as a lower layer. In any case the subsequent crops are contaminated with this double salt and washing and recrystallization must be continued until all calcium chloride has been removed. These latter processes are very time-consuming. In order to obtain the free glycollic acid the calcium is precipitated quantitatively from the solution of the pure calcium glycollate with the calculated amount of oxalic acid and the solution thus obtained evaporated and crystallized. The preparation of glycollic acid may be much simplified by using barium carbonate

---

[1] Hofmann, *Ber.*, 17, 1411 (1884).

[2] *Ber.*, 16, 2955 (1883).

for the hydrolysis instead of calcium carbonate, as will be described below.

50 g. of commercial monochloroacetic acid were dissolved in 500 cc. of water. A small amount of a yellow insoluble impurity was removed by filtration and 120 g. commercial barium carbonate were added slowly. The mixture was heated on a water bath with a reflux condenser for about 30 hours, or until no more carbon dioxide bubbles were evolved. The mixture was thoroughly agitated every few hours toward the last. The excess of barium carbonate was filtered off finally and the hot solution treated with 52.1 g. 95% sulfuric acid, *i. e.*, 95% of the calculated amount necessary for complete precipitation of the barium as barium sulfate. After standing on the hot plate for some time the barium sulfate was readily filtered off on a Büchner funnel with suction. The precipitate was washed several times. The filtrate and washings were treated with small amounts of sulfuric acid until the solution showed only a slight positive test for barium. The solution was filtered again and concentrated *in vacuo*. A small amount of barium sulfate separated which was filtered off. The concentration was continued as long as water was distilled over at the bath temperature used at the beginning. The concentrated solution (a syrup) which smelled strongly of hydrochloric acid was placed on the steam bath in an evaporating dish for two hours. Not all of the hydrochloric acid was expelled in this way. The thick straw-yellow syrup weighed 40 g. (calculated yield of glycollic acid 40 g.). A drop or two of this syrup was induced to crystallize by scratching a few moments with a glass rod and this material was used to inoculate the syrup. Crystallization progressed rapidly. 16.5 g (41%) of the crystallized acid were separated in the first crop. Further crops of crystals were not obtained from this syrup. When the mother liquor was heated further on the steam plate, since it was thought necessary to remove more water in order to promote crystallization, a gelatinous anhydride separated.

The above experiment was repeated, using 100 g. of monochloroacetic acid. The almost colorless syrup in this case crystallized spontaneously. The first crop of crystals weighed 30 g. (37.5% of the calculated yield). This filtrate was heated again as above and gave a large amount of a refractive jelly which had the appearance of crystals when submerged in the syrup. This material was heated in water solution with calcium hydroxide until the solution became slightly but permanently alkaline. The first two crops of dry calcium glycollate weighed 40 g.; the third 7.8 g.; the fourth 3.5, or corresponded to 41 g. of glycollic acid. The total yield of glycollic acid is accordingly 88.7% of the calculated amount, assuming that the commercial chloroacetic acid is pure.

In another experiment 200 g. of chloroacetic acid were heated on the water bath in an open flask with 1400 cc. of water and 400 g. barium carbonate (calculated amount 407 g.) until no more carbon dioxide was evolved. Not nearly all the carbonate had gone into solution. The mixture was diluted to about 4000 cc. finally and the heating continued. The carbonate was now completely dissolved. An excess of carbonate was now added and heating was interrupted when no more carbon dioxide was evolved. The water lost by evaporation was supplied from time to time. The barium was nearly completely removed as before and the final filtrate was treated with a pinch of washed animal charcoal to absorb the fine barium sulfate and filtered until clear. This solution was concentrated to a pale yellow syrup by evaporating on the steam bath in wide vessels. Care was taken to remove it before all water was lost. The cool syrup was inoculated and crystallized into a hard cake overnight. The mass was broken in order to permit the hydrochloric acid remaining to be evaporated. The crystal mass was broken up from time to time and finally as it became dry mashed with a pestle. After standing some days the chloride reaction with silver nitrate became weak and the odor of hydrochloric acid was absent. The crystals were dissolved in a little warm water and filtered after adding a pinch of washed animal charcoal, until the solution was clear. On inoculating the cold syrup, brilliant glass-like colorless crystals of pure glycollic acid separated in large quantities. Dried in a desiccator over sulfuric acid they melt at 78°.

The entire preparation may be carried out with almost no attention on any scale. When concentrating the aqueous solution on the water bath the evaporation must be interrupted in time or no crystals can be obtained. In case of failure to obtain crystals the syrup may be treated with excess barium hydroxide, heated until it remains permanently alkaline and treated as before, using greater care at the final stage of the evaporation.

2 g. of the pure glycollic acid were heated nine hours in a steam oven (99°). The residue weighed 1.65 g. 2 g. glycollic acid can theoretically give 1.76 g. glycollylglycollic acid, $CH_2OHCO_2CH_2CO_2H$. The viscous jelly-like syrup was treated with a little ether and then rubbed up with 25 cc. portions of water. A turbid white suspension was obtained which was diluted to 250 cc.; 25 cc. titrated with 0.1 *N* potassium hydroxide required 12.70 cc. or 127 cc. for all. This much alkali is equivalent to 1.68 g. glycollylglycollic acid. Another specimen of this thick syrup obtained from 2 g. glycollic acid weighed 1.60 g. and on standing a few days separated jelly-like turbid masses which had the same appearance under the microscope as those obtained in the crystallization of glycollic acid above, and which had no resemblance to the beautifully formed crystals of glycollic acid. It is thought that it is in part this anhydride formed so easily at 100° that prevents the crystallization of those glycollic acid syrups which were heated too long after the removal of water.

Other anhydride derivatives of glycollic acid may be formed but will not be discussed here.

It has been shown above that the method of preparation of glycollic acid is rather flexible and requires very little attention. The main advantage is that the time-consuming fractional crystallizations can be avoided by this method. It was found by experience that the method possesses no apparent advantage for the preparation of α-hydroxybutyric acid from α-bromobutyric acid.

CHICAGO, ILL.

[HARRIMAN RESEARCH LABORATORY, THE ROOSEVELT HOSPITAL, NEW YORK.]

LEUCINE ANHYDRIDE, A PRODUCT OF THE WATER HYDROLYSIS OF PROTEIN AT HIGH TEMPERATURES.

BY S. S. GRAVES AND J. T. W. MARSHALL, with the assistance of H. W. ECKWEILER.

Received November 1, 1916.

The hydrolysis of protein has been of interest for nearly a century but with the more exhaustive results obtained by acid, alkali and enzyme digestions, the original method of heat hydrolysis with water has practically fallen into disuse. Recently, however, an ether-soluble crystalline substance[1] has been noted among the products of protein hydrolyzed at high temperatures with water.

With the idea of identifying and studying this substance, its preparation and purification were undertaken. Preliminary experiments showed that small amounts of the substance could be prepared by autoclave digestion of protein with water, and that by prolonged heating at high temperatures, the yield was markedly increased. Several grams were thus obtained by the ether extraction of hydrolyzed casein. The crystals from the ether residue were contaminated by a yellowish oil, which was removed by repeated crystallizations from boiling acetone and the substance was finally obtained in the form of fine white needles which melted at 272° (corr.) and sublimed unchanged. Further attempts at purification did not change the melting point nor was it possible to isolate any other crystalline substance from the ether extract. The solubility of the purified substance was found to be 0.3% in acetone at 20°, 0.6% in boiling acetone, 1.4% in chloroform at 20° and its solubility in ethyl and methyl alcohol and in glacial acetic acid was of about this order, while in ether it was very much less. In cold water the pure substance was practically insoluble.

Contrary to expectations the substance was found to have a slight optical activity.

0.2662 gram of substance in 10 cc. of glacial acetic acid.
$\alpha_D = +0.151°$ in 2 dm. tube by Na light.
$[\alpha]_D^{20} = +2.83°$.

---

[1] Private communication from Dr. S. R. Benedict.