to 95% of the theoretical yield (about 8.25 g.). It follows that the reaction between glycolic nitrile and liquid ammonia, under the conditions noted, is smooth, clean, and, allowing for unavoidable loss through indirect measure of yield, practically quantitative.

The same method, with modified technique in individual cases, was successfully applied to the preparation of other known aminonitriles, desired for pharmacological investigation. Further study of the method and its application was interrupted by the author's change in affiliation and field of activity and has not been resumed because of lack of opportunity.

LAFAYETTE COLLEGE
EASTON, PENNA.

RECEIVED JULY 23, 1934

COMMUNICATIONS TO THE EDITOR

OXIDATION OF CYSTINE WITH PERMONOSULFURIC ACID

Sir:

Sulfur oxides of cystine [Toennies and Lavine, *J. Biol. Chem.*, **100,** 463 (1933)] should be obtainable in presence of water if oxygenation is rapid compared with speed of hydrolysis of the —S—S— bond. As cystine disulfoxide [Lavine, Toennies and Wagner, THIS JOURNAL, **56,** 242 (1934)] proved to be relatively stable toward aqueous acids the action on cystine of a potent oxygen donor such as permonosulfuric acid (prepared from $K_2S_2O_8$ and H_2SO_4 [Gleu, *Z. anorg. allgem. Chem.*, **195,** 70 (1931)]) seemed interesting. The following is a preliminary report on this investigation. In presence of 10.7 mole equivalents of H_2SO_5 oxygen consumption stopped after two hours at 5.0 atoms, the theoretical amount for oxidation to cysteic acid, suggesting that absence of free electron pairs in the acid form ($-NH_3^+$) protects the amino group against oxygen addition. The speed of oxygen consumption with different H_2SO_5 : cystine ratios (cystine 0.025 *M*, H_2SO_4 3.5 *M*, 0°) was as follows:

		Atoms O consumed per mol. of cystine, after min.					
	H_2SO_5:cystine	2	9	13	20	30	70
I	1.01:1	0.75	1.00	1.01			
II	2.10:1	1.2	1.7	1.9	2.0	2.10	
III	5.37:1	2.6	3.8	4.0	4.2	4.3	4.5

After oxidation I the direct cyanide–nitroprusside test indicated 15% of unchanged cystine while by a preceding reduction with iodide [Toennies and Lavine, *J. Biol. Chem.*, **105,** 119 (1934)] the test was increased to 93% of the cystine used. After oxidation II the corresponding figures were 5 and 95%. Thus the chief reaction products seem to be the monosulfoxide in oxidation I and the disulfoxide in oxidation II.

By diluting the H_2SO_5 solution (Ref. 3) with methanol the potassium sulfate present was nearly completely precipitated and the filtrate (0.1 *M* H_2SO_5, 0.9 *M* H_2SO_4, 75% CH_3OH), in which H_2SO_5 is as stable as in aqueous solution, was used to oxidize cystine, dissolved as perchlorate in CH_3CN (Ref. 1), with 1 mole equivalent of H_2SO_5. Precipitates obtained—after oxidation—by neutralization with pyridine, contained at least twice as much cystine as was indicated by direct test on the oxidized solution. Further evidence of a dismutative change of the primary oxidation product was obtained by fractionated neutralization of the precipitate, inasmuch as it resulted in further formation of cystine together with a decrease of total precipitate, and by polarimetric observation. On oxidation of cystine with 1 mole of H_2SO_5 the initial high negative rotation decreases in less than one hour to a slightly positive value, only to slowly turn negative again during two to three days, passing through a maximum of about one-third of the initial value and slowly decreasing again during the next two weeks. This last decrease presumably represents esterification (Ref. 1) by methanol of the cystine formed by dismutation during the second stage of change. Addition of ethanol and ether immediately after the first brief reaction stage yielded a white precipitate which, according to analysis and properties, consists of sulfates of cystine (10%) and its monosulfoxide (90%) and which in *N* sulfuric acid gives an initial specific rotation of about +5° for the total content of unoxidized and oxidized cystine. This value however, changes during the next five days to a constant negative level which would correspond to an amount of free cystine equivalent to 70% of the organic sulfur present.

LANKENAU HOSPITAL RESEARCH INSTITUTE
PHILADELPHIA, PENNSYLVANIA G. TOENNIES

RECEIVED JULY 10, 1934

MOLECULAR COMBINATIONS OF β-METHYL-*d*-GLUCOSIDE, β-METHYL-*d*-XYLOSIDE AND β-METHYL-*l*-FUCOSIDE WITH POTASSIUM ACETATE[1]

Sir:

While engaged in deacetylating tetraacetyl-β-methyl-*d*-glucoside with an alcoholic solution of potassium hydroxide, we observed the separation of a quantity of long silky needle-like crystals; these proved to represent a molecular combination of β-methyl-*d*-glucoside with potassium acetate ($C_7H_{14}O_6 \cdot CH_3COOK$). The same substance was prepared in quantity by mixing concentrated absolute alcohol solutions of the glycoside and of the anhydrous salt.[2] The α-methyl-*d*-glucoside when similarly treated in many experiments over a period of two years has never yielded any crystalline product. This specificity of the reaction constitutes its chief usefulness since it affords a convenient method of separating the beta form completely from its alpha isomer, a process which formerly was accomplished only by tedious fractionation. Application of this new double compound for such separations will be reported later.

The compound contains the sugar derivative and the salt in a molecular ratio of one to one as is indicated by the methoxyl and potassium analyses. It melts at 181–182° (corr.) and shows $[\alpha]^{20}_{D}$ in water $-22.0°$, which is the specific rotation that would be calculated on the assumption that the salt is inert and has no influence upon the rotation of the sugar derivative. The silky needles are rather hygroscopic.

The analogous compound of β-methyl-*l*-fucoside ($C_7H_{14}O_5 \cdot CH_3COOK$) is almost identical in superficial appearance, is similarly hygroscopic, melts at 208–212° (corr.) and shows $[\alpha]^{20}_{D}$ in water $+8.9°$. It is also a one to one molecular combination as indicated by its analyses and its specific rotation. This substance has been particularly valuable in facilitating the separation of β-methyl-*l*-fucoside from the alpha isomer, which forms no analogous compound, since the separation by fractionation was especially difficult in this case.

The β-methyl-*d*-xyloside potassium acetate compound ($C_6H_{12}O_5 \cdot CH_3COOK$), which is also of very similar appearance, is hygroscopic, melts at 171–172° (corr.), shows $[\alpha]^{20}_{D}$ in water $-41.3°$ and is likewise a one to one combination.

The glycoside may be recovered in each case by precipitating the potassium as potassium acid tartrate from a solution containing 50% of alcohol. By treating the double compounds directly with acetic anhydride, the acetylated methylglycosides may be obtained almost quantitatively, the salt acting as catalyst.

Efforts to prepare similar derivatives of α- and β-methyl-*d*-arabinoside, α- and β-methyl-*d*-galactoside, α- and β-methyl-*d*-lyxoside, α-methyl-*d*-xyloside, α-methyl-*d*-glucoside and α-methyl-*l*-fucoside have been unsuccessful. Other communications will follow.

NATIONAL INSTITUTE OF HEALTH
WASHINGTON, D. C.
A. J. WATTERS
R. C. HOCKETT
C. S. HUDSON

RECEIVED AUGUST 27, 1934

A NEW SYNTHESIS OF N-MONOPHENYLPIPERAZINE

Sir:

The only reported synthesis of N-monophenylpiperazine is that of V. Prelog and G. J. Driza [*Coll. Czechoslovak Chem. Comm.*, **5**, 497–502 (1933)].

The same synthesis had been accomplished by us in this Laboratory previous to the publication by the above authors. Since we had also noticed the physiological effects of N-monophenylpiperazine, it was decided to find, if possible, an easier and more convenient method for preparing it. This was desirable in view of the fact that we encountered considerable difficulty in preparing the intermediate bis-(β-haloethyl)-amines in sufficient quantities to make any large amounts of the N-monophenylpiperazine.

We have been able to prepare N-monophenylpiperazine in practically any amount by heating together aniline hydrochloride and diethanolamine hydrochloride at about 240° for from six to eight hours. In practice, the amines are mixed in molecular proportions and concd. hydrochloric acid added until the solution is neutral to litmus. The water is then boiled off and when the temperature has reached 220 to 240° it is kept there for from six to eight hours. Upon cooling the mass sets to a dark brown, gummy solid. The free base is liberated by treatment with concd. sodium hydroxide and the resulting oil is then fractionated

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[1] Publication authorized by the Surgeon General, U. S. Public Health Service.

[2] The samples of commercial potassium acetate which we examined all contained a molecule of acetic acid of crystallization per molecule of salt, though the labels described the substance as CH_3COOK. The salt may be dried by heating at 150° but the same products are obtained from the methyl glycosides by using either the dried or the undried salt.

in a vacuum, b. p. 156–157° (uncorr.) at 10 mm. (uncorr.). The yields are above 50% but vary considerably with the time of heating. Bis-(β-phenylaminoethyl)-amine is also formed but in smaller amounts.

N-Monophenylpiperazine is insoluble in water and soluble in all common organic solvents, d_4^{20} 1.0621; *neut. eq.* calcd. 162.1; found, 165.0. The hydrochloride of N-monophenylpiperazine was used for analysis for nitrogen. Calcd.: N, 14.11. Found: N, 14.01.

Other mono N-substituted amines have been prepared by this same method and their properties and derivatives will form the basis of a forthcoming publication.

ORGANIC CHEMISTRY LABORATORY C. B. POLLARD
UNIVERSITY OF FLORIDA L. G. MACDOWELL
GAINESVILLE, FLORIDA

RECEIVED AUGUST 20, 1934

THE ISOLATION OF 0.1 GRAM OF THE OXIDE OF ELEMENT 91 (PROTACTINIUM)

Sir:

Using a process described previously [A. V. Grosse, *Ber.*, **61,** 233 (1928); THIS JOURNAL, **52,** 1742 (1930)] we have recently been able to work up large quantities of radium residues from Joachimsthal, Czechoslovakia. Thanks to the courtesy of the Lindsay Light Company, a small plant for the treatment of these residues was rigged up at their factory in West Chicago.

The technical process of concentration consists briefly: (1) an extraction of the residues, consisting principally of SiO_2, Fe_2O_3 and PbO with hydrochloric acid; (2) a melt of the silica residue, containing the protactinium, with sodium hydroxide, and (3) separation of the protactinium with zirconium phosphate from the mixture of basic oxides remaining after the melt is leached.

The starting material contains on the average 0.3 g. of protactinium per metric ton or a concentration of 1 part in 3 millions. The plant product contains the element in a concentration of 1 part in 5000, the yield being about 75%.

The plant product is further concentrated in the laboratory by a series of fractional crystallizations of zirconium oxychloride and zirconium phosphate precipitations. At a concentration of about 10% by weight of protactinium, most of the zirconium can be separated by sublimation of the chlorides; protactinium is then best precipitated directly by means of hydrogen peroxide. The purity of the oxide obtained by this method has been proved by x-ray analysis [H. Beuthe and A. V. Grosse, *Z. Physik,* **61,** 170 (1930)].

A detailed description of the technical and laboratory process will be given later.

Up to the present time, the plant product from about 1 ton of residues was worked up and 0.1 g. of protactinium oxide (Pa_2O_5) isolated in the pure state. Larger quantities will be isolated in the near future.

This work required by its very nature large financial expenditures and it has been made possible only by a generous grant of Mr. Hiram J. Halle of New York City, to whom we express our sincere gratitude. We are much indebted to Mr. A. C. Ratchesky, U. S. Minister to Czechoslovakia, and to Mr. Frank Novotny, U. S. Legation in Prague, for their efficient support in obtaining the raw material from the Czechoslovakian Government, and to Prof. Julius Stieglitz for his continuous help and advice.

KENT CHEMICAL LABORATORY A. V. GROSSE
UNIVERSITY OF CHICAGO M. S. AGRUSS
CHICAGO, ILL.

RECEIVED SEPTEMBER 10, 1934

METALLIC ELEMENT 91

Sir:

Isolation from radium residues of about 0.1 g. of protactinium oxide has been accomplished recently [A. V. Grosse and M. S. Agruss, THIS JOURNAL, **56,** 2200 (1934)]. The pure oxide (Pa_2O_5) was converted into the metal by two methods: (1) By bombarding the oxide, on a copper target, with a stream of electrons in a high vacuum. The use of 35,000-volt electrons for a few hours at a current strength of 5–10 milliamperes, splits the oxide into oxygen and the metal, the latter remaining as a shiny, partly sintered, metallic mass, stable in air. (2) By transforming it into a halide (Cl, Br, I) and then cracking it in a high vacuum (10^{-6} to 10^{-5} mm.) on an electrically heated tungsten filament, according to the reaction $2PaX_5 \longrightarrow 2Pa + 5X_2\uparrow$, the general method first introduced by Langmuir [I. Langmuir, THIS JOURNAL, **37,** 1139 (1915)]. The protactinium formed a shiny gray white, partly molten, deposit on the filament. The metal does not oxidize in air, in an expected contrast to metallic radium [Marie Curie and A. Debierne, *Compt. rend.*, **151,** 523 (1910)], and retains its luster for quite a while.

The yield of the metal from the pentachloride is poor as compared to the iodide.

The pentachloride can be prepared readily at 550°, by reaction of the oxide with phosgene, according to the equation $Pa_2O_5 + 5COCl_2 \longrightarrow 2PaCl_5 + 5CO_2\uparrow$. Under these conditions the oxide is volatilized quantitatively; the pentachloride sublimes in beautiful transparent nearly colorless long needles, reaching a length of 1 cm. and more, if sublimed slowly. The chloride melts at 301° at atmospheric pressure to a pale yellow liquid, but sublimes appreciably below its melting point. The substance is ideally suited for an atomic weight determination of protactinium, which is under way.

The present experiments are of a preliminary nature; M. Agruss and the writer are planning to prepare larger amounts of the metal and study its properties quantitatively.

We take this opportunity to express our sincere gratitude to Mr. Hiram J. Halle of New York City, who made this work possible by a generous financial grant. We are very much indebted to Dr. Gustav Egloff for placing at our disposal for this work the facilities of the Research Laboratories of the Universal Oil Products Company. It is also a pleasure to acknowledge the assistance of M. Agruss and L. Borst.

KENT CHEMICAL LABORATORY
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS
RESEARCH LABORATORIES OF THE
UNIVERSAL OIL PRODUCTS COMPANY
RIVERSIDE, ILLINOIS
A. V. GROSSE

RECEIVED SEPTEMBER 10, 1934

THE EFFECT OF FRACTIONAL CRYSTALLIZATION ON THE ISOTOPIC COMPOSITION OF WATER

Sir:

In a recent communication Professor G. Bruni [THIS JOURNAL, **56,** 2013 (1934)] has discussed the possibility of separating the isotopic species present in ordinary water by fractional crystallization. His conclusion, based on experiment, is that "*if* a fractionation takes place it amounts to less than $^1/_{10{,}000}$ ..... when the original mass is reduced to $^1/_{14{,}300}$." The figure probably refers to change in specific gravity.

I have recrystallized distilled water by freezing half the amount taken and advancing the fractions as was done by Richards and Hall [*ibid.*, **39,** 531 (1917)]. The water was thoroughly stirred during the two hours required for freezing. Samples were further purified and specific gravities were taken in the way already described [E. S. Gilfillan, Jr., THIS JOURNAL, **56,** 406 (1934)]. Blank runs were made between each two determinations; the average deviation of these from the mean was 0.1 p. p. m. The results are given in Table I.

TABLE I

Crystns.	10	10	8	12	8	12
Sp.-gr., 1, p. p. m.	1.2	1.0	0.9	1.1	0.7	1.3

The average effect per crystallization is 0.10 p. p. m. The effect was also determined for 6% sodium chloride solutions and found to be 0.5 ± 0.3 p. p. m.

The experiments of La Mer, Eichelberger and Urey [THIS JOURNAL, **56,** 248 (1934)] permit an approximate thermodynamic calculation of the effect to be expected due to concentration of deuterium. The following assumptions are made: (1) In mixtures of protium and deuterium oxides the molecular species H^1H^2O, H^1H^2O, and H^2H^2O, are present in mobile equilibrium. (2) The equilibrium constant $K_c = [H^1H^2O]^2/[H^1H^1O][H^2H^2O] = 4$. (3) These species form "perfect solutions" in the sense of Lewis [G. N. Lewis and M. Randall, "Thermodynamics," McGraw-Hill Book Co., 1923, p. 221] in both liquid and solid phases. (4) The heats of fusion of the three kinds of water are the same. (5) The freezing point of deuterium oxide is 3.82°. (6) The specific gravity of ordinary water is 22.2 p. p. m. higher than that of H^1H^1O. The first two assumptions have been made by Lewis and Cornish [THIS JOURNAL, **55,** 2616 (1933)]. The result is that one crystallization should change the specific gravity of ordinary water by 0.22 ± 0.01 p. p. m. This indicates that fractional crystallization concentrates O^{16} with respect to O^{18} and that the freezing point of $H^1H^1O^{18}$ is $-0.1 \pm 0.05°$.

From each of the measurements of La Mer, Eichelburger and Urey the freezing point of H^1H^2O can be calculated. The values found are 2.20, 2.21 and 2.28, average 2.23°. From this value one can calculate the freezing point of the water studied by Washburn, Smith and Frandsen [*Bur. Standards J. Research,* **11,** 453 (1933)] to be 0.053° in agreement with the value found.

EDWARD SMITH GILFILLAN, JR.
National Research Fellow
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RESEARCH LABORATORY OF PHYSICAL CHEMISTRY
OF THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASS.

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