ride (1 g.), sodium acetate (1.5 g.) and some alcohol was refluxed for four hours. The product gave colorless prisms from alcohol, m. p. 184°; yield, 2 g.

Anal. Calcd. for $C_{16}H_{18}O_2N_2$: N, 10.37. Found: N, 10.21.

Beckmann Change with the Oxime.—Thionyl chloride (11 g.) was added dropwise into the ice cold suspension of the oxime (1 g.) in chloroform (50 cc.). The resulting solution, after standing, was shaken with ice water. Subsequent to removal of chloroform the residual yellow oil (1 g.) was dissolved in ether and treated with concd. sodium bisulfite. After being dried with potassium carbonate, and removal of ether, 0.5 g. of oil which soon turned to colorless prisms was obtained. It was pressed on a tone plate and crystallized from ether, m. p. 75–76°. Folin found the same m. p. for his specimen of *p*-dimethylaminobenzonitrile.[2]

(2) Folin, *Am. Chem. J.*, **19**, 333 (1897).

Anal. Calcd. for $C_9H_{10}N_2$: C, 73.97; H, 6.85; N, 19.18 Found: C, 74.23; H, 6.78; N, 19.26.

On working up the bisulfite solution, 0.4 g. of benzaldehyde was obtained. It was identified by converting it into phenylhydrazone which alone or mixed with a known specimen melted at 155–156°.

Anal. Calcd. for $C_{13}H_{12}N_2$: N, 14.29. Found: N, 14.28.

***p*-Dimethylaminobenzoic Acid.**—A solution of the nitrile (0.2 g.) and potassium hydroxide (1 g.) in alcohol (9 cc.) and water (1 cc.) was refluxed for eight hours until liberation of ammonia had ceased. The product gave colorless prismatic needles from alcohol, m. p. 235° (dec.).

Anal. Calcd. for $C_9H_{11}O_2N$: N, 8.48. Found: N, 8.64.

CHEMICAL LABORATORY OF
KITASATO INSTITUTE
TOKYO, JAPAN

RECEIVED SEPTEMBER 17, 1934

COMMUNICATIONS TO THE EDITOR

THE ISOMERIZATION OF NORMAL HEPTANE

Sir:

C. D. Nenitzescu and A. Dragan have reported [*Ber.*, **66**, 1892 (1933)] that *n*-hexane and *n*-heptane heated on a water-bath in the presence of aluminum chloride yield a large amount of isohexane and isoheptane, respectively. The data presented by these authors do not substantiate these statements with great certainty: the starting materials were not very pure, the products obtained boiled over wide ranges, and the assertion regarding the compounds formed is based only on these boiling ranges, without the corroborating evidence of other physical properties. A. D. Petrow, A. P. Meschtscherjakow and D. N. Andrejew [*ibid.*, **68**, 1 (1935)] state that *n*-heptane is isomerized in 25% yield by heating for six hours at 300–400° in the presence of zinc chloride. In this case the density of the fractions obtained is obviously too high to correspond to any of the branched-chain heptanes. We have repeated the work of Nenitzescu and Dragan, using 2650 g. of pure *n*-heptane from Jeffrey pine. The product boiling from 50 to 98.4° was carefully fractionated, and the following properties determined for the fractions: $n^{20}D$, average molecular weight (by vapor density), and critical temperature of solution in aniline. A comparison of these data with the properties of *n*-hexane and all the heptanes indicates the presence of *n*-hexane and 2-methylhexane, and of no other isomeric heptane.

We estimate that the *n*-hexane found represents about 1% and the 2-methylhexane about 4% of the *n*-heptane consumed in the reaction.

A further investigation of this reaction is in progress.

RESEARCH LABORATORIES
ETHYL GASOLINE CORPORATION
DETROIT, MICHIGAN
GEORGE CALINGAERT
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RECEIVED JANUARY 18, 1935

ERGOTOCIN: THE ACTIVE PRINCIPLE OF ERGOT RESPONSIBLE FOR THE ORAL EFFECTIVENESS OF SOME ERGOT PREPARATIONS ON HUMAN UTERI

Sir:

It has been found by the authors, working in conjunction with Drs. Davis, Adair and Rogers of the Department of Obstetrics and Gynecology of The University of Chicago, that the alkaloids ergotoxine, ergotamine and sensibamine are uniformly ineffective when administered orally to human mothers in doses of 2 mg. Larger doses (2–4 mg.) often induce unpleasant side reactions such as nausea, vomiting, increase in blood pressure, diarrhea, etc. However, even

these large and dangerous doses do not induce contractions in the eighth-day postpartum uterus, in all mothers. While the number of cases studied by us is relatively small (15 cases) these large doses of the alkaloids were found effective only in about 30% of the cases.

We have found, however, that *some* fluid extracts of ergot prepared in accordance with U. S. P. method, were effective in doses corresponding to 3–4 g. of ergot. The activity of these extracts could of course not be due to the known alkaloids (the amounts of these alkaloids as assayed by us were too small to account for the activity), and we undertook the problem of the isolation of the principle responsible for the efficacy of oral ergot dosage. While preparations containing 60–80% of this principle were obtained by us over a year and one-half ago, the isolation of the pure crystalline substance was made only Dec. 12, 1934. We have called this principle ergotocin. In human mothers this substance is uniformly effective when administered orally in doses of 0.3 mg. and intravenously in doses as low as 0.1 mg. The yield of 0.3 mg. of ergotocin is roughly equal to 3–4 g. of crude defatted ergot. This principle thus accounts for the activity of the fluid extracts.

Ergotocin has now been used on over 150 patients and no unpleasant symptoms have been observed with it. It controls uterine hemorrhage instantly. Intravenously the effect is noticed within fifteen seconds after administration. In the first stages the action of ergotocin resembles that of pituitary extracts, except that its effect lasts for three or four hours, in marked contrast to the transient effect usually obtained with pituitary extract. In its low toxicity, small dosage, prompt action in uterine hemorrhage, prolonged effect on the uterine muscles, ergotocin is unique among oxytocic principles.

Ergotocin salts, as well as the free base, are white, well-defined crystalline substances. The base melts with decomposition at 155°. The picrate, which is red, melts at 195–197°, with decomposition. When heated with alkali, ergotocin (or its salts) does not liberate any ammonia. Under the same experimental conditions, however, the known alkaloids (ergotoxine, ergotamine, sensibamine) eliminate quantitatively one mole of ammonia. The free base is somewhat soluble in water, and the salts are readily soluble. One may obtain even a 10% aqueous solution of some salts of ergotocin, a unique property among the alkaloids isolated from ergot. Ergotocin differs from the known ergot alkaloids (ergotoxine, ergotamine, sensibamine) in that it is not precipitated by Meyers' reagent in dilutions greater than 1 part in 7500, while the other alkaloids are precipitated in dilutions of 1:200,000 to 1:2,000,000. The optical rotation of the salts of ergotocin so far investigated is positive. The chemistry of ergotocin as well as some of the attempts to synthesize it will be reported as soon as the work now under way is complete.

We believe that with the isolation of this principle ergot therapy can now be put on a rational basis. If one bears in mind that many ergots do not contain this principle (and yet are acceptable on the basis of the U. S. P. assays), the cause of the difference of opinion among obstetricians regarding the value of ergot in obstetrics becomes evident.

The authors wish to take this opportunity to thank most sincerely the Research Corporation, Inc., for a grant which made this work possible and the Eli Lilly Co. for generously aiding us in this investigation.

Needless to say, without the coöperation and constant guidance of Drs. Davis, Adair and Rogers, on the clinical and pharmacological evaluation of this principle, this work would not have been brought to a successful conclusion.

GEORGE HERBERT JONES CHEMICAL LABORATORY
THE UNIVERSITY OF CHICAGO M. S. KHARASCH
CHICAGO, ILLINOIS R. R. LEGAULT

RECEIVED MARCH 30, 1935

THE SURFACE TENSION OF SOLUTIONS

Sir:

It has long been known that aqueous solutions of most salts have a slightly greater surface tension than water throughout the range of concentrations hitherto investigated and must, therefore, according to the Gibbs Theorem, be negatively adsorbed in the surface layer. According to Freundlich and earlier authors such "capillary inactive substances" give surface tension–concentration (σ–c) curves which are approximately straight lines with a gentle positive slope. Wagner [*Physik. Z.*, **25**, 47 (1924)] and later Onsager and Samaras [*J. Chem. Phys.*, **2**, 528 (1934)] have applied the Debye–Hückel theory of interionic attraction to the problem and derived an equation

$$\frac{\sigma}{\sigma_0} = 1 + \frac{79.517}{D\sigma_0} c \log \frac{1.143 \times 10^{-18} (DT)^3}{c}$$