ture, and depends upon the geometry of the apparatus. The effect of the wall separation of the convection column has not been investigated. Equation (2) must be regarded as only approximately verified by the experimental data, but it represents their trend quite satisfactorily.

For runs of sufficient duration, the linear dependence of log C_B/C_A on time must finally fail, since a stationary state must eventually be approached in the apparatus. From the data we conclude that the durations of the experiments were short relative to the time required to approach closely the stationary state, and that this state evidently corresponds to a rather high concentration of the proteins in the bottom reservoir.

In the representative fractionations of Table VI, it will be observed that the transport of each component of the mixture is nearly that which would occur if it were transported alone under the same conditions. It also appears that the separation factor does not depend to a marked degree on the initial composition of the protein solutions. To the extent that these approximations are valid, we may estimate the separation factor by the equation

$$\log f = \Delta\beta lEt \qquad (3)$$

where $\Delta\beta$ is the difference of the transport coefficients β of equation (2) for the individual proteins of the mixture. We surmise that $\Delta\beta$ is approximately proportional to $\Delta\mu$ the difference of the electrophoretic mobilities of the proteins, but the data are not sufficient to permit a definite conclusion on this point.

The representative separation factor 1.5 obtained in the series of exploratory runs indicates that the method has practical possibilities. By suitable modifications in design, it is hoped that batch operation in a single unit may be replaced by continuous operation in a series of fractionating units of the type described.

Acknowledgment.—The writers wish to express their thanks to Professor E. J. Cohn of the Harvard Medical School for a supply of the bovine serum albumin,[2] and to Dr. C. L. Hoagland of the Rockefeller Institute for Medical Research for a supply of the azo-ovalbumin. They also wish to thank Dr. T. Shedlovsky and Dr. D. A. McInnes of the Rockefeller Institute and Professor J. B. Sumner of Cornell University for helpful suggestions.

Summary

An electrophoresis convection apparatus has been described for the fractionation of protein mixtures in which an electric field is used to transport the proteins in a horizontal direction while the density gradient thus developed brings about convection currents in a vertical direction.

Factors affecting the concentrating of proteins by this method are discussed, and pertinent data are presented.

The partial separation of horse hemoglobin and bovine serum albumin has been accomplished. Horse hemoglobin and an azo-ovalbumin have also been partially separated.

(2) The protein was prepared in the course of work carried out under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

ITHACA, NEW YORK RECEIVED OCTOBER 23, 1945

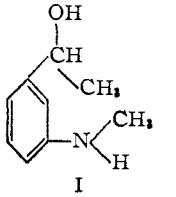
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Some Derivatives of *m*-Ethylaniline. A Novel Disproportionation of an Aminophenylmethylcarbinol[1]

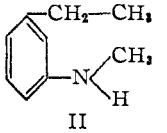
BY C. S. MARVEL AND C. G. OVERBERGER

The desire to obtain styrene derivatives containing basic groups led us to attempt the dehydration of *m*-N-methylaminophenylmethylcarbinol (I) over activated alumina at 450–500°. To our surprise the only product isolated in these experiments was *m*-N-methylaminoethylbenzene (II). That this was obtained in yields of 40–50% suggests that a disproportionation reaction occurred and half of the starting material was reduced whereas the other half was oxidized and lost probably as tar during the reaction.

The following evidence indicates that an ethylbenzene rather than a styrene derivative was obtained. The analytical data on II and its picrate agree with the proposed structure; the base (II) did not take up hydrogen over an Adams platinum oxide catalyst[2] and the picrate obtained from a sample before this treatment was identical with one prepared after the treatment; the carbinol (I) was reduced readily by hydrogen over a copper



I



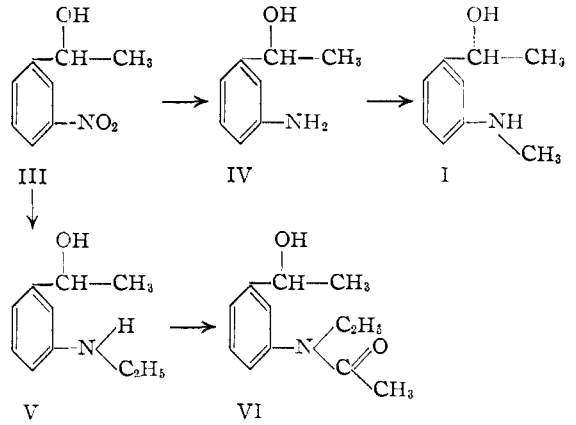
II

(1) The work described in this manuscript was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

(2) Adams, Voorhees and Shriner, "Organic Syntheses," 2nd ed., Coll. Vol. I, John Wiley and Sons, Inc., New York, 1941, p. 463.

chromium oxide catalyst[3,4] to give a compound whose picrate proved to be identical with the one prepared from the product obtained in the attempted dehydration.

The *m*-N-methylaminophenylmethylcarbinol (I) was synthesized by catalytic reduction of *m*-nitrophenylmethylcarbinol (III) to the amino carbinol (IV) and subsequent alkylation with dimethyl sulfate. Two other related derivatives were prepared from the nitrocarbinol which further served to characterize the series. Reductive alkylation[5] converted the nitro carbinol (III) into the *m*-N-ethylamino derivative (V) which was characterized as an acetate (VI). Attempted dehydration of this acetate gave no identifiable products.



Experimental[6]

m-**Nitrophenylmethylcarbinol** (III).—The reduction of 500 g. of *m*-nitroacetophenone by the method of Lund[7] gave 250 g. (50%) of the desired carbinol melting at 61–62°. Lund[7] reported that the pure carbinol melts at 62.5°.

m-**Aminophenylmethylcarbinol** (IV).—One hundred grams of *m*-nitrophenylmethylcarbinol, dissolved in 400 cc. of absolute alcohol, was hydrogenated over Raney nickel catalyst in a large bomb. The temperature never exceeded 50°. After the theoretical amount of hydrogen had been absorbed, the bomb was opened, rinsed with absolute ethanol, and the solution filtered to remove the catalyst. The alcohol solution was dried over sodium sulfate, filtered and the alcohol removed. The residue was recrystallized from a mixture of benzene and high-boiling petroleum ether. The yield was 77.5 g. (94%) of a white solid melting at 63–64°.

Anal. Calcd. for $C_8H_{11}NO$: C, 70.03; H, 8.08. Found: C, 70.04; H, 8.30.

m-**N-Methylaminophenylmethylcarbinol** (I).—In a 1-liter, three-necked, round-bottomed flask equipped with stirrer, condenser and dropping funnel, a solution of 40 g. of *m*-aminophenylmethylcarbinol in 200 cc. of water was cooled with stirring in an ice-bath. To this with stirring was slowly added 70 g. of freshly distilled dimethyl sulfate. The addition took about fifteen minutes. To this cooled reaction mixture a sodium hydroxide solution was added (about 40 g. of sodium hydroxide dissolved in 270 cc. of water) with stirring (one hour). The reaction mixture was then stirred and allowed to come to room temperature over a period of three to five hours. The mixture was then stirred for two hours at 50°. After cooling, the mixture was extracted with 500 cc. of ether and dried over sodium sulfate. The ether solution was filtered and the ether removed. The residue was distilled in a 50-cc. Claisen flask. The yield was 25 g. (57%) of a slightly colored, viscous liquid boiling at 140–142° (1.5–2 mm.), $n^{20}D$ 1.5650. About 12 g. of product was distilled in a three-plate column for analyses. A Hinsberg[8] test indicated a secondary amine.

Anal. Calcd. for $C_9H_{13}NO$: C, 71.48; H, 8.66. Found: C, 71.56; H, 8.95.

m-**N-Methylaminoethylbenzene** (II).—Fourteen grams of *m*-N-methylaminophenylmethylcarbinol was slowly dropped (2 drops per minute or less) onto hot, activated alumina (450–500°) in a vertical tube 12 mm. in diameter packed eight inches in depth with "Hydralo".[9] The addition took about one and one-half hours. The product was collected in a 25-cc. filter flask packed in ice. The product was a dark-colored, evil-smelling liquid. A small layer of water could be detected in the bottom of the filter flask. The product was dissolved in 40 cc. of ether, and a few crystals of hydroquinone were added. The ether solution was washed with 25 cc. of 10% sodium hydroxide solution and then with 25 cc. of a saturated calcium chloride solution. The ether solution was dried over sodium sulfate, filtered and the ether removed. The residue was distilled in a 15-cc. modified Claisen flask. The yield was 6 g. (48%) of a slightly colored liquid boiling at 81–85° (1 mm.), $n^{20}D$ 1.5575.

Anal. Calcd. for $C_9H_{13}N$: C, 79.9; H, 9.68; N, 10.36. Found: C, 80.12, 80.57, 80.14, 80.49; H, 9.31, 10.00 9.99, 9.42; N, 10.23.

A picrate was prepared in the usual manner[10] and recrystallized from 95% ethanol, m. p. 133–134°.

Anal. Calcd. for $C_{15}H_{16}N_4O_7$: N, 15.38. Found: N, 14.92.

Attempted Hydrogenation over Platinum Oxide.—In a 125-cc., round-bottomed flask equipped with ground-glass joint were placed 0.5 g. of the compound obtained from the attempted dehydration, 0.14 g. of platinum oxide (Adams catalyst), and 20 cc. of 95% ethanol. Slightly more hydrogen reacted than was necessary to reduce the platinum oxide, but the discrepancy between the calculated amount and the actual amount was not great, and little, if any, reduction of the compound in question took place. The platinum oxide was filtered, and the alcohol evaporated to a volume of 10 cc. About 9 cc. of a saturated solution of picric acid in methanol was added and the solution evaporated slightly. A yellow picrate separated, which upon recrystallization from 95% ethanol melted at 133–134°. The picrate of the compound obtained from the attempted dehydration reaction, prepared in a similar manner in alcoholic solution, melted at 132–133°. The mixed melting point was 132–133°.

Hydrogenation of *m*-**N-Methylaminophenylmethylcarbinol.**—In a small, high-pressure hydrogenation bomb 0.63 g. (0.0041 mole) of *m*-N-methylaminophenylmethylcarbinol was dissolved in 20 cc. of 95% ethanol and hydrogenated over copper chromium oxide catalyst at 200°. The mixture was filtered, the alcoholic solution was evaporated to about 8 cc. and 8 cc. of a saturated alcoholic picric acid solution was added. The yellow picrate obtained on recrystallization from 95% ethanol melted at 133–134°. The

(3) Adkins, "Reactions of Hydrogen with Organic Compounds over Copper Chromium Oxide and Nickel Catalysts," The University of Wisconsin Press, Madison, Wisconsin, 1937, p. 12.

(4) This reaction was carried out by Dr. J. M. Stewart.

(5) The general method of Emerson and Mohrman, THIS JOURNAL, **62**, 69 (1940), was used.

(6) Microanalyses were done by Mr. H. S. Clark, Illinois State Geological Survey and Miss Theta Spoor, University of Illinois.

(7) Lund, *Ber.*, **70**, 1520 (1937).

(8) Shriner and Fuson, "The Systematic Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, 1941, p. 48.

(9) "Hydralo"-activated alumina from the Sterling Products Company.

(10) Ref. 8, page 149.

mixed melting point of the picrate with the one from the product obtained by dehydration of the carbinol was not depressed.

Anal. Calcd. for $C_{15}H_{16}N_4O_7$: N, 15.38. Found: N, 15.19.

m-N-Ethylaminophenylmethylcarbinol (V).—The general procedure of Emerson and Mohrman[5] was employed. In a 300-cc. magnesium citrate bottle were placed 16.7 g. of *m*-nitrophenylmethylcarbinol, 2 g. of sodium acetate, 13.2 g. of acetaldehyde and 3–5 g. of Raney nickel. After complete reduction the Raney nickel was removed by filtration, and the alcohol was removed by evaporation. About 80 cc. of ether was added to the resulting slush, and any solid material was filtered. The resulting ether solution was dried over sodium sulfate, the solvent removed, and the residue distilled in a 25-cc., modified Claisen flask. The slightly yellow product boiled at 135–138° (2 mm.), $n^{20}D$ 1.5620. The yield was 12 g. or 73% of the theoretical amount.

Anal. Calcd. for $C_{10}H_{15}ON$: C, 72.68; H, 9.15. Found: C, 72.82; H, 9.01.

m-N-Ethyl-N-acetylaminophenylmethylcarbinol (VI).—In a 300-cc. Erlenmeyer flask was placed 6 g. of *m*-N-ethylaminophenylmethylcarbinol suspended in 60 cc. of water. To this was added 5 g. of concentrated hydrochloric acid and the suspension shaken well until the *m*-N-ethylaminophenylmethylcarbinol dissolved. This solution was then heated to 50° and 6 g. of acetic anhydride was added, immediately followed by 6 g. of sodium acetate. The resulting solution was well mixed and allowed to stand at 50°, for one to two hours. The solution was cooled, extracted with 400 cc. of ether and dried over sodium sulfate. The ether was removed and the residue distilled in a 10-cc. modified Claisen flask. The slightly yellow, viscous oil boiled at 160–162° (0.5 mm.), $n^{20}D$ 1.5390. The yield was 3 g. or 40% of the theoretical. Considerable resinification occurred at the high temperature necessary for distillation. Usually the excess acetic acid and starting material, *m*-N-ethylaminophenylmethylcarbinol, were removed by distillation and the crude residue used in the subsequent attempted dehydration.

Anal. Calcd. for $C_{12}H_{17}O_2N$: C, 69.53; H, 8.26. Found: C, 69.56; H, 8.35.

Summary

Attempted dehydration of *m*-N-methylaminophenylmethylcarbinol over activated alumina led to a disproportionation product, *m*-N-methylaminoethylbenzene. Attempts to dehydrate two related carbinols gave no identifiable products.

URBANA, ILLINOIS RECEIVED NOVEMBER 16, 1945

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF WINTHROP CHEMICAL COMPANY, INC.]

Water-Insoluble Forms of Thiamine and Niacin

BY WOLFGANG HUBER, WERNER BOEHME AND S. C. LASKOWSKI

The need for water-insoluble forms of thiamin, niacin and riboflavin for the enrichment of corn grits and white rice has been pointed out by the Food and Nutrition Board of the National Research Council.[1] Since these cereals are customarily rinsed before cooking, the water-soluble vitamins previously sprayed on the exterior surfaces of the particles are removed, thus obviating this standard method of enrichment.

The present report describes several avenues of approach which have been pursued in these laboratories in order to obtain water-insoluble forms of thiamine and niacin without losing the biological activity. In the case of thiamine, salts were prepared with various derivatives of high-molecular carboxylic and sulfonic acids, including a number of anionic wetting agents. Thus, salts were prepared with several alkylsulfuric acids,[2] with cholestenone-6-sulfonic acid and with methane-1,1-bis-(2-hydroxy-3-naphthoic acid). With the wetting agents only thiamine 2-ethylhexylsulfate was isolated in crystalline form, while all alkyl sulfates of higher molecular weight separated as oils. The thiamine salts of isopropylnaphthalenesulfonic acid and di-octylsulfosuccinic acid also separated in non-crystalline form while the thiamine salt of dibutylsulfosuccinic acid was found to be water-soluble. With cholestenone-6-sulfonic acid as well as with methane-1,1-bis-(2-hydroxy-3-naphthoic acid), thiamine formed water-insoluble solids which could be purified from organic solvents to give well defined crystalline compounds.

In the niacin series neither the acid nor the amide formed satisfactory salts with methane-1,1-bis-(2-hydroxy-3-naphthoic acid) or 2-ethylhexylsulfuric acid. Apparently, the basicity of the ring nitrogen is so far reduced by the presence of a carboxyl in the β-position that a salt will not form.

The preparation and the water solubilities of a series of *n*-alkyl esters of nicotinic acid have recently been reported.[3] Prior to this publication a series of alkyl nicotinates had been prepared in these laboratories and the compounds investigated for their possible value as water-insoluble derivatives. We find that our data are in good agreement with those of Badgett, *et al.*, except for some preparatory details which will be reported in the experimental part. From a practical point of view the enrichment of cereals with alkyl nicotinates has some objections, since these compounds are odoriferous, somewhat unstable oils. However, esterification increased the basicity of the ring nitrogen sufficiently to allow the formation of salts with methane-1,1-bis-(2-hydroxy-3-naphthoic acid). These are odorless, pale yellow solids of very low water solubility, which can be purified by recrystallization from organic solvents.

(1) Gunderson, *Science*, **98**, 277 (1943).

(2) Tergitol series of wetting agents, Carbide & Carbon Chemicals Corp., New York, N. Y.

(3) Badgett, Provost, Ogg and Woodward, THIS JOURNAL, **67**, 1135 (1945).