Preparation of *m*-Aminophenyl β-Piperidinoethyl Ketone Mono-hydrochloride

In connection with a problem in this Laboratory, we had occasion to prepare *m*-aminophenyl β-piperidinoethyl ketone mono-hydrochloride. Mannich[1] was not able to obtain this compound by chemical reduction of the nitro base because of the unstable nature of the amine in acid solution and the nitro base was not reduced by catalytic hydrogenation. However, we have obtained the *m*-aminophenyl β-piperidinoethyl ketone mono-hydrochloride by catalytic reduction of *m*-nitrophenyl β-piperidinoethyl ketone mono-hydrochloride in aqueous solution with palladium on charcoal.

Following a procedure of Mannich,[2] the *m*-nitrophenyl β-piperidinoethyl ketone hydrochloride was prepared. The melting point of the crude material was 178–179°, softens at 175°. When recrystallized from alcohol–acetone and from 12A absolute alcohol the m. p. was 180–181°[3] (literature[1] m. p. 171–172°). *Anal.* Calcd. for $C_{14}H_{19}ClN_2O_3$: N, 9.35. Found: N, 9.43.

***m*-Aminophenyl β-Piperidinoethyl Ketone Mono-hydrochloride.**—Twelve grams (0.04 mole) of *m*-nitrophenyl β-piperidinoethyl ketone hydrochloride was dissolved in 100 ml. of water and hydrogenated in a Parr shaker in the presence of 1.2 g. of 5% palladium on activated charcoal (American Platinum Works, Newark, New Jersey) under 20 lb. pressure of hydrogen. The reduction was complete in thirty minutes. The solution was filtered from the catalyst and concentrated under reduced pressure to a sirup. About 50 ml. of absolute alcohol was added and the mass triturated. After a short period the soft mass crystallized. Eight grams of material, m. p. 175–178° (dec.), was obtained on filtering. (A mixed m. p. with starting material showed a depression of 18°.) An additional two grams of lower m. p. was obtained on addition of several volumes of dry ether. The total yield of crude material was 10 g. (92.5%). After treating with Darco and crystallizing three times from absolute alcohol, an analytical sample had m. p. 176–177° (dec.). *Anal.* Calcd. $C_{14}H_{21}ClN_2O$: C, 62.55; H, 7.50; N, 10.42. Found: C, 62.34; H, 7.74; N, 10.42.

We wish to thank E. F. Shelberg, Chief Microanalyst, for the microanalyses here reported.

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(1) Mannich and Dannehl, *Arch. Pharm.*, **276**, 206 (1938).

(2) "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1942, Vol. I, p. 329.

(3) Melting points are uncorrected.

COMMUNICATIONS TO THE EDITOR

THE NUCLEOTIDE COMPOSITION OF RIBONUCLEIC ACIDS[1]

Sir:

In continuation of our nucleic acid studies, procedures have been developed[2] that permit the separation on filter paper and estimation by spectrophotometry of all ribonucleotides encountered in ribonucleic acids. The separations were performed in an ammonia atmosphere with isobutyric acid as solvent. The components were demonstrated on the chromatograms by the previously described indirect method[2] or directly by inspection under the "Mineralight."[3] Although uridylic acid shared its position on the chromatogram with guanylic acid, the complete nucleotide analysis of ribonucleic acids could be effected by either of the following procedures. *Procedure 1:* 6–20 mg. of ribonucleic acid was kept at *p*H 13.5 for twelve to fifteen hours at 30°. The solution was brought to *p*H 3 to 4 (final volume 1 cc.) and submitted to separation in 0.01-cc. portions. Guanylic acid was eluted together with uridylic acid and the extinction at 265 and 245 mμ determined. The concentrations of the two components were calculated by simultaneous equations based on the absorption of the pure nucleotides. *Procedure 2:* 6–14 mg. of ribonucleic acid was suspended in absolute methanol and the purines liberated by gaseous hydrogen chloride.[4] The evaporation residue of the total hydrolysate was brought to *p*H 13.5. The rest of the operations followed Procedure 1. In this manner uridylic and cytidylic acids, guanine, and adenine could be separated and quantitatively determined on one chromatogram without supplementary calculations.

TABLE I

NUCLEOTIDE COMPOSITION OF RIBONUCLEIC ACIDS (EXPRESSED AS PER CENT. OF NUCLEIC ACID PHOSPHORUS)

Source	Procedure (see text)	Guanylic acid	Adenylic acid	Cytidylic acid	Uridylic acid	Total
Yeast Prepn. 1	1	28.0	29.0	17.8	20.3	95.1
	2	28.8	25.8	16.5	19.5	90.6
	3	25.6	26.1	24.4	8.3	84.4
Yeast Prepn. 2	1	27.3	26.2	19.6	15.3	88.4
	2				18.8	
	3	30.6	24.6			
Yeast Prepn. 3	1	26.2	24.8	21.4	20.3	92.7
	3	25.9	24.2			
Pig pancreas	2	40.7	18.9	17.8	8.4	85.8
	3	40.2	16.6	20.5	4.6	81.9
Pig liver	1	31.1	18.5	26.5	12.9	89.0
	3	31	17			

(1) This work was supported by a research grant from the U. S. Public Health Service.

(2) Vischer, Magasanik and Chargaff, *Federation Proc.*, **8**, in press (1949).

(3) We are very grateful to Dr. C. E. Carter, Oak Ridge National Laboratory, for suggesting this instrument.

(4) Vischer and Chargaff, *J. Biol. Chem.*, **176**, 715 (1948).

The results are summarized in Table I and compared with the quantities of free purines and pyrimidines found in acid hydrolysates of nucleic acids (*Procedure 3*).[4] It will be seen that the nucleotide analyses presented here contribute to a more complete understanding of ribonucleic acid composition, mainly with respect to uridylic acid which has proved relatively resistant to formic acid hydrolysis.[4] They also reveal remarkable differences between ribonucleic acids from different sources.

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RECEIVED MARCH 17, 1949

REARRANGEMENT OF 2-BROMOBICYCLO[2,2,2]OCTANE WITH SILVER BROMIDE

Sir:

We have found that the brominative decarboxylation[1] of a suspension of the silver salt of bicyclo[2,2,2]octane-2-carboxylic acid[2] (I) affords 2-bromobicyclo[1,2,3]octane (II), m. p. 39–41°. The structure of II is tentatively assigned on the grounds (a) that reduction with sodium and alcohol gives bicyclo[1,2,3]octane (III) [*Anal.* Calcd. for C_8H_{14}: C, 87.19; H, 12.81. Found: C, 86.88; H, 13.14], m. p. 139.5–141°, reported 133°[3,4] and 141°[5] and (b) that aqueous alcoholic alkali gives an alcohol, m. p. 183–184°, which is apparently identical with the bicyclo[1,2,3]octane-2-ol, m. p. 183°, of Alder and Windemuth[5] by virtue of the similarity of the phenylurethan [*Anal.* Calcd. for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.62; H, 7.74; N, 5.64], m. p. 128–129.5°, reported[5] 130° and the hydrogen phthalate [*Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.11; H, 6.74], m. p. 118–119°, reported[5] 116–117°.

This rearrangement, the first example of the conversion of the bicyclo[2,2,2]octane system to the bicyclo[1,2,3]octane system,[6] has prompted examination of the effect of silver bromide on the potentially initial product, 2-bromobicyclo[2,2,2]-octane (IV). Unrearranged IV [*Anal.* Calcd. for $C_8H_{13}Br$: C, 50.81; H, 6.93; Br, 42.26. Found: C, 50.90; H, 6.89; Br, 42.13], m. p. 64–65.5°, is prepared from bicyclo[2,2,2]octene[2] by the addition of hydrogen bromide in ether,[7] and can be reduced to bicyclo[2,2,2]octane (V), m. p. 169.5–170.5°. On treatment in carbon tetrachloride either with silver bromide or with silver acetate and bromine but not with bromine alone, IV is converted in good yield to II (identified by reduction to III).

The silver bromide-catalyzed rearrangement affords strong experimental support to the hypothesis that silver bromide is a Lewis acid of sufficient strength to weaken *observably* the carbon–bromine bond of an alkyl bromide. Limiting the establishment of a mechanism for the brominative decarboxylation is the corollary hypothesis that the alkyl bromide actually *isolated*, having been subject to alteration by silver bromide, is not necessarily identical with the bromide produced initially in the decarboxylation. Consequently, the rearrangement observed in the decarboxylation of I may not, in the absence of further experimentation, form the basis for a mechanistic hypothesis. Similarly no mechanistic significance is attributable to the optical inactivity of the 3-bromoheptane isolated from the brominative decarboxylation of optically active silver heptane-3-carboxylate,[8] in the absence of observations on the optical stability of 3-bromoheptane in the presence of silver bromide.

(1) *Cf.* Kleinberg, *Chem. Rev.*, **40**, 381 (1947).
(2) Seka and Tramposch, *Ber.*, **75**, 1379 (1942).
(3) Komppa, *et al.*, *Ann.*, **521**, 242 (1936).
(4) Barrett and Linstead, *J. Chem. Soc.*, 611 (1936).
(5) Alder and Windemuth, *Ber.*, **71**, 2404 (1938).
(6) The driving force is plausibly derived from the relief of Pitzer strain [Beckett, Pitzer and Spitzer, THIS JOURNAL, **69**, 2488 (1947)].
(7) Following Meerwein and von Emster, *Ber.*, **55**, 2500 (1922).
(8) Arnold and Morgan, THIS JOURNAL, **70**, 4248 (1948).

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VITAMIN B_{12}. V. IDENTIFICATION OF CRYSTALLINE VITAMIN B_{12a}

Sir:

Catalytic reaction of vitamin B_{12} with hydrogen has yielded a crystalline product which shows high hematopoietic activity in pernicious anemia, although it is somewhat less active than vitamin B_{12}.

To a solution of 26.3 mg. of vitamin B_{12} in 15 ml. of water, 78 mg. of platinum oxide catalyst was added and the mixture was shaken with hydrogen at atmospheric pressure for twenty hours. During reaction, the red color changed to dark brown, but on contact with air the red color returned indicating changes in the cobalt ion. The filtrate from the catalyst was evaporated *in vacuo* at 25°. The residue was dissolved in 1 ml. of water and 6 ml. of acetone was added. After several hours, 1–2 mg. of precipitate formed and was removed. Acetone (2 ml.) was added again and, after standing, 4–5 mg. of precipitate was removed. Acetone (2 ml.) was added, and dark-red crystals formed during twenty-four hours; yield, 12 mg. Further addition of acetone yielded more crystalline material.

After two recrystallizations from water by the addition of acetone, the red crystals showed refractive indices[1a] of α, 1.580; β, 1.640; and γ, 1.654. The cobalt (4.58%) and phosphorus (2.43%) content reveal that the B_{12} molecule is not grossly altered.

(1) Courtesy of (a) Dr. Charles Rosenblum; (b) Mr. David Hendlin; (c) Dr. Gladys Emerson; (d) Dr. Walther Ott.