concentration of potassium hydroxide necessary for the formation of the latter named acid. For acetaldehyde, McLeod[1] has found that vinyl alcohol molecules are present in the aqueous solution of the aldehyde as soon as the concentration of the alkali is above 0.1%. In the case of alcohol, as the amount of potassium hydroxide was increased to about 250 g., the oxalic and carbonic acids simultaneously increased, although at different rates. Beyond this concentration of potassium hydroxide, the curves become practically straight lines, parallel to the X-axis. It required two drops of potassium permanganate solution (strength = 0.089 *N*) to give a slight permanent color to the distillate containing acetic acid when it had been previously made alkaline with sodium carbonate. This may be taken as an indication of a mere trace of either formic acid or formaldehyde or both. The total amount of alcohol recovered as oxidation products, in some instances, was slightly higher than that demanded by theory, but this was undoubtedly due to the absorption of slight amounts of carbon dioxide during the process of oxidation.

Series of experiments at 25° and 75° will be completed within a short time and it is hoped that an early report of the same will be made in THIS JOURNAL. We hope to present a discussion of our results at that time.

TABLE I.

Actually used (grams).			C_2H_5OH calc. for 30 g. $KMnO_4$.	Actually found with proper correction for CO_2 and CH_3COOH (grams).			Calc. for 5 g. alcohol (grams).			
$KMnO_4$.	KOH.	C_2H_5OH.		CO_2. Ave. of two.	$(COOH)_2$. Ave. of two.	CH_3COOH. Ave. of two.	KOH.	CO_2.	$(COOH)_2$.	CH_3COOH.
31.18	None	6.17	5.94	0.088	None	7.400	None	0.071	None	6.000
30.00	5.3	5.02	5.02	0.632	0.975	5.228	5.3	0.629	0.951	5.207
30.41	10.7	4.83	4.76	0.768	1.259	4.873	11.2	0.795	1.303	5.044
30.00	21.3	4.37	4.37	0.828	1.700	4.042	24.4	0.947	1.959	4.624
30.27	42.6	4.07	4.04	1.058	1.996	3.356	52.3	1.300	2.451	4.121
30.30	85.2	3.65	3.61	1.269	2.195	2.564	112.1	1.737	3.000	3.512
30.00	170.4	3.34	3.34	1.184	1.999	2.110	258.1	1.772	2.992	3.519
31.97	255.6	3.51	3.29	1.307	2.077	2.198	388.4	1.863	2.959	3.131
35.38	340.8	3.89	3.28	1.335	2.370	2.440	579.3	1.716	3.049	3.139

COLUMBUS, O.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON AMINES. THE FORMATION OF SCHIFF BASES FROM β-PHENYLETHYLAMINE AND THEIR REDUCTION TO ALKYL DERIVATIVES OF THIS AMINE.

[FIFTH PAPER.]

BY NORMAN A. SHEPARD AND ARTHUR A. TICKNOR.

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While working in coöperation with Professor Treat B. Johnson on an investigation dealing with the relationship between chemical constitution

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[1] *Am. Chem. J.*, 37, 24 (1907).

and the therapeutic action of certain organic bases, the writers were assigned the problem of synthesizing several N-substituted derivatives of β-phenylethylamine. Certain aromatic representatives of this class of compounds were desired in order to compare their pharmacological activity with that of β-phenylethylamine (I) and its *p*-hydroxy derivative, namely, *p*-hydroxyphenylethylamine or *tyramine* (II).

$$\underset{\text{(I).}}{C_6H_5CH_2CH_2NH_2} \qquad\qquad \underset{\text{(II).}}{HOC_6H_4CH_2CH_2NH_2}$$

As is well known, both of these two bases (I and II) are physiologically active and, when injected subcutaneously, cause an increase in the blood pressure of the organism and also produce a strong contraction of the uterus.

We now give a description in this paper of the preparation and properties of five bases of this type, which have been incorporated in our work, namely: benzylphenylethylamine (IV), *p*-methoxybenzylphenylethylamine (X), *p*-hydroxybenzylphenylethylamine (VIII), *o*-hydroxybenzylphenylethylamine (VI), and 3-methoxy-4-hydroxybenzylphenylethylamine (XII). These were all prepared by reduction, with sodium and alcohol, of their corresponding Schiff bases, which were obtained by condensation of β-phenylethylamine (I) with the proper aromatic aldehyde.

$$\underset{\text{(III).}}{C_6H_5CH_2CH_2N : CHC_6H_5} \longrightarrow \underset{\text{(IV).}}{C_6H_5CH_2CH_2NHCH_2C_6H_5}$$

$$\underset{\text{(V).}}{C_6H_5CH_2CH_2N : CHC_6H_4OH\ (o)} \longrightarrow \underset{\text{(VI).}}{C_6H_5CH_2CH_2NHCH_2C_6H_4OH\ (o)}$$

$$\underset{\text{(VII).}}{C_6H_5CH_2CH_2N : CH.C_6H_4.OH\ (p)} \longrightarrow \underset{\text{(VIII).}}{C_6H_5CH_2CH_2NHCH_2C_6H_4OH\ (p)}$$

$$\underset{\text{(IX).}}{C_6H_5CH_2CH_2N : CHC_6H_4(OCH_3)\ (p)} \longrightarrow$$

$$\underset{\text{(X)}}{C_6H_5CH_2CH_2NHCH_2C_6H_4OCH_3\ (p)}$$

$$\underset{\text{(XI).}}{C_6H_5CH_2CH_2 : NCHC_6H_3(OCH_3)(OH)} \longrightarrow$$

$$\underset{\text{(XII).}}{C_6H_5CH_2CH_2NH.CH_2C_6H_3(OCH_3)(OH)}$$

Of these representatives of the two series, only (III), (IV) and (XI) have hitherto been described. Benzalphenylethylamine (III) was apparently first prepared by Walpole and Barger.[1] They gave, however, no description of its properties and assigned to it a melting point which we were unable to confirm. The Schiff base (XI) has been described by Decker and Becker,[2] and the alkyl amine benzylphenylethylamine (IV), was prepared by Fischer.[3] The Schiff bases (III), (V), (VII),

[1] *J. Chem. Soc.*, **95**, 1723 (1909).

[2] *Ann.*, **395**, 367 (1913).

[3] *Ber.*, **29**, 211 (1896).

(IX) and (XI) were all solids and stable at high temperatures in the absence of water. The amines (III) and (IX) were distilled under diminished pressure without decomposition. The *p*-hydroxybenzal derivative (VII) was characterized by its high melting point (190°) which was 145° higher than that of the *o*-derivative (45°).

The transformations from the Schiff bases to the alkyl derivatives of phenylethylamine were nearly quantitative in the cases of benzylphenylethylamine (IV), *p*-methoxybenzylphenylethylamine (X) and *p*-hydroxybenzylphenylethylamine (VIII). The latter base is also formed quantitatively by heating its corresponding methyl ether with hydriodic acid. All three of these amines gave stable hydrochloric acid salts which were characterized by their crystalline character and insolubility in cold water. While *o*-hydroxybenzalphenylethylamine and 3-methoxy-4-hydroxyphenylethylamine undergo reduction with formation of their corresponding amines (VI) and (XII), respectively, the yields, however, were small because part of the Schiff bases underwent a normal hydrolysis with formation of β-phenylethylamine and the corresponding aldehyde.

Experimental Part.

Benzal-β-phenylethylamine, $C_6H_5CH_2.CH_2N : CHC_6H_5$.—Barger and Walpole[1] prepared this substance by condensation of benzaldehyde with phenylethylamine. The compound was not analyzed by them, but they state that it melts at about 70° and on nitration is transformed into *p*-nitrophenylethylamine, $NO_2C_6H_4CH_2CH_2NH_2$. We have prepared the compound by the same method and find that it is easily purified by distillation under diminished pressure. Our base boiled at 188–189° at 17–19 mm. pressure and, on cooling, solidified in the form of stout, colorless prisms which melted sharply at 41–42°. The yield of purified material was 91% of the theoretical.

Calc. for $C_{15}H_{15}N$: N, 6.70. Found: N, 6.8.

Benzyl-β-phenylethylamine, $C_6H_5CH_2CH_2NH.CH_2C_6H_5$.—This base has been described by Fischer[1] and was prepared by two methods. It was obtained from benzylphenylhydroxyethylamine, $C_6H_5CH_2NH.CH_2.CHOH.C_6H_5$ by reduction with hydriodic acid and phosphonium iodide, and also by reduction of the Schiff base, phenylethylidenebenzylamine, $C_6H_5CH_2N : CH.CH_2C_6H_5$, with sodium and alcohol. The yield by the latter method was 25% of the theoretical. We find that practically a quantitative yield of the same base is obtained by reduction of the above benzal derivative with sodium and alcohol. Our procedure was to dissolve 15 g. of the unsaturated compound in 300 g. of absolute alcohol and then reduce the double bond by slowly introducing 40 g. of metallic sodium. After the sodium had dissolved the alcohol solution was carefully diluted with water and finally acidified strongly with hydrochloric acid. On

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[1] *Loc. cit.*

evaporating this solution the base was obtained in the form of its difficultly soluble hydrochloric acid salt. This crystallized from hot water in the form of glistening plates, which melted at 265–266° to a clear oil (Fischer assigned 264–266° as the melting point). From 15 g. of the Schiff base we obtained 18 g. of the hydrochloride.

***p*-Methoxybenzal-β-phenylethylamine,** $C_6H_5CH_2CH_2N:CHC_6H_4.OCH_3$.—This compound is easily obtained by condensation of anisic aldehyde with phenylethylamine. From 8.1 g. of the amine we obtained 13 g. of the unsaturated compound boiling at 224–225° at 17 mm. pressure. This oil solidified on cooling to a colorless crystalline mass which melted at 34–35° to an oil.

Calc. for $C_{16}H_{17}ON$: N, 5.85. Found: N, 5.77.

***p*-Methoxybenzyl-β-phenylethylamine,** $C_6H_5CH_2CH_2NHCH_2C_6H_4.OCH_3$.—Working under similar conditions as were employed for the preparation of benzylphenylethylamine from benzalphenylethylamine, we were successful in reducing the above *p*-methoxybenzalphenylethylamine to this base by the action of sodium and alcohol. It was obtained in the form of its hydrochloride which crystallized from hot water in the form of plates. They melted at 266–267° to a clear oil without effervescence. The yield was excellent.

Calc. for $C_{16}H_{19}ON.HCl$: N, 5.04. Found: N, 4.94.

The free base is obtained as a colorless oil insoluble in water when the above salt is decomposed with alkali.

***p*-Hydroxybenzal-β-phenylethylamine,** $C_6H_5CH_2CH_2N:CHC_6H_4OH$.—*p*-Hydroxybenzaldehyde condenses smoothly with phenylethylamine at 100° forming this unsaturated derivative. It was obtained in the form of deep yellow crystals which separated from 95% alcohol in yellow prisms. They melted at 188–190° to a clear oil. The base is readily soluble in alcohol and difficultly soluble in benzene, from which it deposits in clusters or burrs of light yellow prisms. The yield of purified material was 83.0% of the theoretical.

Calc. for $C_{15}H_{15}ON$: N, 6.22. Found: N, 6.30.

***p*-Hydroxybenzyl-β-phenylethylamine,** $C_6H_5CH_2CH_2NH.CH_2C_6H_4OH$.—*p*-Hydroxybenzalphenylethylamine is reduced smoothly by sodium and alcohol using the same proportions as previously given. The residue obtained, after the reaction mixture was acidified with hydrochloric acid and the solution evaporated, was treated with just enough water to dissolve the sodium chloride and leave the hydrochloride of the base undissolved. This salt was then separated and purified by crystallization from dilute hydrochloric acid, in which it was quite difficultly soluble. On cooling, it separated in leaflets which melted at 225–226° to a clear oil. The compound was purified for analysis by recrystallization from

50% alcohol and separated, on cooling, as clusters of long prisms. The yield of purified material was 4.9 g. or 64.5 % of the theoretical.

Calc. for $C_{15}H_{18}ONCl$: N, 5.3. Found: N, 5.5.

The free base was obtained by decomposing the hydrochloride with ammonia. It separated in a crystalline condition and crystallized from alcohol in hexagonal tables which melted at 135–136° to a clear oil. The amine was moderately soluble in ether and difficultly soluble in benzene. Nitrogen determinations in the free base after drying over concentrated sulfuric acid:

Calc. for $C_{15}H_{17}ON$: N, 6.17. Found: N, 6.2, 6.3.

This same amine was also formed by heating *p*-methoxybenzyl-β-phenylethylamine with hydriodic acid. Four grams of the methoxy compound were suspended in 35 cc. of hydriodic acid and the mixture boiled for one hour. Methyliodide was evolved and a clear solution was obtained. On adding water to the hydriodic acid solution the hydriodide separated in the form of plates. The free base was obtained by treatment of this salt with ammonia and crystallized from alcohol as hexagonal prisms or tables melting at 135–136°. This base dissolves in sodium hydroxide solution and responds to Millon's test for a phenol group. An attempt to prepare the hydroxy base by heating *p*-methoxybenzyl-β-phenylethylamine with hydrochloric acid was unsuccessful. For example, the ether was recovered unaltered after heating with concentrated hydrochloric acid for 2 hours at 130–145°.

o-**Hydroxybenzal-β-phenylethylamine,** $C_6H_5CH_2CH_2N : CH.C_6H_4.OH$.—Eight grams of salicylic aldehyde were mixed with an equivalent weight of phenylethylamine at ordinary temperature. On standing there was an energetic reaction, with evolution of heat and formation of water. After heating at 100° for one hour to complete the reaction, this condensation product was obtained as an oil, which solidified on cooling. It was purified for analysis by recrystallization from hot alcohol and separated on cooling in the form of yellow prisms melting at 45.5° to a clear oil. The compound is very soluble in ether. The yield was practically quantitative.

Calc. for $C_{15}H_{15}ON$: N, 6.2. Found: N, 6.2, 6.17.

o-**Hydroxybenzyl-β-phenylethylamine,** $C_6H_5CH_2CH_2NH.CH_2C_6H_4OH$.—Fifteen grams of the preceding condensation product, dissolved in 20 parts of absolute alcohol, were reduced at the boiling temperature of the alcohol with 2.5 parts of sodium. After the sodium had completely dissolved, the nearly colorless solution was cooled, diluted with water and then combined with 300 cc. of dilute hydrochloric acid (1 part water to 1 part concentrated acid). On evaporating to dryness at 100° a brown oil, soluble in alcohol and insoluble in ether, separated and was removed mechanically from a crystalline residue. This crystalline product, which was identified as the hydrochloride of the above amine (2.7 g.) mixed with sodium chloride, was triturated with cold water to remove the sodium salt and then purified as follows: The free base was first liberated from its salt by treatment with ammonia and finally extracted with ether. On saturating this ether solution with hydrochloric acid gas the salt deposited at once as stout prisms or blocks. These melted at 130° to a clear oil. The salt is easily dissociated by heating and also when warmed with water. Nitrogen determination after drying to constant weight at 97°:

Calc. for $C_{15}H_{18}ONCl$: N, 5.3. Found: N, 5.6.

From the aqueous solution above, containing the sodium chloride, we recovered 2.5 g. of phenylethylamine, which was formed by hydrolysis of the unreduced Schiff base. When alcohol containing 1–2% of water was used as the solvent, practically no reduction took place by addition of sodium and phenylethylamine was the only base obtained.

3-Methoxy-4-hydroxybenzal-β-phenylethylamine, $C_6H_5CH_2CH_2N:CHC_6H_3(OCH_3)(OH)$.—This base was prepared by condensing vanillin with phenylethylamine according to the directions of Decker and Becker.[1] In crystalline form, however, and also color and melting point our product did not agree with the description given by these investigators. Our compound separated from alcohol as stout, yellow columns or prisms which melted at 112–113° to a clear oil, and the compound retained its yellow color after repeated crystallizations. Decker and Becker state that their product crystallized in colorless plates which melted at 108–109°.

Calc. for $C_{16}H_{17}O_2N$: N, 5.50. Found: N, 5.6, 5.7.

From the alcoholic filtrates left after crystallization of the above compound a small amount (0.3 g.) of a dark red, crystalline substance was obtained, which deposited from hot alcohol in rectangular plates. The color was not removed by repeated crystallizations from alcohol and benzene. The compound melted at 220–221° to a red oil. It was practically insoluble in hot water, sodium hydroxide solution and hydrochloric acid and difficultly soluble in alcohol and benzene. This product, which contained 8.57% of nitrogen, was not examined further. This same substance was also formed during the condensation of *p*-hydroxybenzaldehyde with β-phenylethylamine. The quantity obtained, however, was very small (less than 0.5 g.).

3-Methoxy-4-hydroxybenzyl-β-phenylethylamine, $C_6H_5CH_2CH_2NH.CH_2C_6H_3(OCH_3)(OH)$.—When 7.2 g. of 3-methoxy-4-hydroxybenzal-β-phenylethylamine were reduced with sodium and alcohol and treated in a similar manner as described under the preparation of *o*-hydroxybenzyl-β-phenylethylamine, 3.9 g., or 47% of the theoretical quantity, of the

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[1] *Loc. cit.*

hydrochloride of the above base were obtained. This salt crystallized from dilute hydrochloric acid as clusters of slender needles, which melted at 180° to a colorless oil.

Calc. for $C_{16}H_{20}ONCl$: N, 4.78. Found: N, 4.73, 4.49.

In order to obtain the free base the hydrochloride was decomposed by ammonia and the amine extracted with ether. After drying the ether solution over sodium sulfate the solvent was then evaporated, when the amine was obtained as a solid. It crystallized from 95% alcohol in the form of needles and melted at 99–100° to a clear oil. It was dried for analysis over concentrated sulfuric acid.

Calc. for $C_{16}H_{19}O_2N$: N, 4.34. Found: N, 4.5, 4.6.

Part of the Schiff base underwent hydrolysis during the above operation and we recovered 1.2 g. of the hydrochloride of phenylethylamine.

NEW HAVEN, CONN.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA.]

A NEW CASE OF TAUTOMERISM: 1,4,5,6-TETRAHYDROXYNAPHTHALENE.[1]

BY A. S. WHEELER AND V. C. EDWARDS.

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Zincke and Schmidt[2] reduced 5,6-dihydroxy-α-naphthoquinone (naphthazarine) with stannous chloride, obtaining a yellow compound, melting at 154°, which they designated 1,4,5,6-tetraoxynaphthalin. Its phenolic character was indicated by the easy preparation of a tetracetyl derivative, colorless prisms melting at 277–9° with decomposition, and also by the fact that its solutions show a strong greenish fluorescence. A peculiar behavior of the solutions was noted in that they soon turn red if exposed to the air and deposit red crystals, which melt at the same temperature as the yellow compound, 154°. The deep color is retained after recrystallization. Heating and the presence of oxidizing agents hasten the change from yellow to red, but ultimate analysis indicates no change in composition and the two forms yield the same derivatives. The authors attributed the color to the presence of a highly colored oxidation product in slight amount. This peculiarity and the results obtained by Willstätter and Wheeler[3] on the hydrojuglones led to the study of this phenol.

The Badische Anilin u. Soda-Fabrik, Ludwigshafen am Rhein, gener-

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[1] This paper forms Part I of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of North Carolina by V. C. Edwards. Part II on The Bromination of 1,4,5,6-Tetrahydroxynaphthalene will appear later.

[2] *Ann.*, 286, 27 (1895).

[3] *Ber.*, 47, 2796 (1914).