hypobromite was substituted for potassium hypobromite with improved yield. As in the α-methyl series solution could not be effected with sodium hypochlorite when tried on the *p*-methoxy amide. The methoxyamines are liquids having a faintly fishy ammoniacal odor which becomes more intense on standing.

β-Methyl-β-hydroxyphenethylamines.—The methoxyamines were demethylated and purified as described in the previous paper. No difficulty was encountered in the crystallization of their hydrochlorides from absolute alcohol–ether. The free bases have not as yet been isolated.

The authors wish to thank Mr. C. H. Emerson for the microanalyses given. The detailed pharmacological results will appear elsewhere.

Summary

The three monomethoxy and corresponding β-hydroxyphenyl β-methylethylamine hydrochlorides have been prepared in a pure state for the purpose of pharmacological testing.

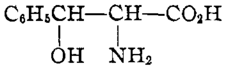
KALAMAZOO, MICH. RECEIVED FEBRUARY 23, 1938

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

β-Phenylnaphthalene[1]

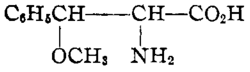
BY HERBERT E. CARTER AND EDWARD J. VAN LOON

In connection with attempts to synthesize phenylserine (I) the corresponding methoxy acids (II) were subjected to treatment with hydrobromic acid.



$\underset{OH}{C_6H_5CH}-\underset{NH_2}{CH}-CO_2H$

I



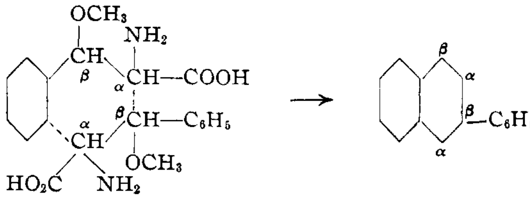
$\underset{OCH_3}{C_6H_5CH}-\underset{NH_2}{CH}-CO_2H$

II

It had been reported earlier by Schrauth and Geller[2] that this reaction gave a brominated hydrocinnamic acid and traces of cinnamic acid. However, we found the reaction to take an entirely different course. The two amino acids (II) behaved in the same manner when refluxed with hydrobromic acid. Each yielded a white crystalline hydrocarbon which was shown to be β-phenylnaphthalene by its analysis, melting point, and oxidation to β-phenylnaphthoquinone.

Elucidation of the mechanism of this reaction offers an interesting problem. The following facts must be explained satisfactorily: (1) The yield of β-phenylnaphthalene is 80 to 85% of the theoretical amount and the reaction is complete in one hour. Therefore, the intermediate steps must proceed smoothly and rapidly. (2) Carbon dioxide is evolved almost quantitatively during the reaction. Therefore, some intermediate must be decarboxylated readily. (3) As a corollary of (2) no phenylnaphthoic acids are isolated from the reaction product.

It is obvious on inspecting the formula of β-phenylnaphthalene that the naphthalene nucleus must arise from two molecules of the aminomethoxy acid with the elimination of two molecules each of methyl alcohol, ammonia, and carbon dioxide.



Furthermore, the α,β union of the two molecules suggests an aldol condensation of a carbonyl-containing intermediate.

The fact that phenylserine, when refluxed with hydrobromic acid, yielded β-phenylnaphthalene in exactly the same manner as the aminomethoxy acids indicated that demethylation was the first step in the reaction. A survey of the literature disclosed that phenylserine yields phenylacetaldehyde under the influence of moderately concentrated sulfuric acid[3] and that phenylacetaldehyde, when heated with strong mineral acids, gives β-phenylnaphthalene in poor yields.[4] More recently Bettzieche[5] reported that refluxing phenylserine with 10% sulfuric acid for twelve hours produced phenylacetaldehyde (identified by the oxime), β-phenylnaphthalene (characterized by its physical properties), and an acidic fraction giving a ferric chloride enol test which the author considered to be sufficient evidence for the presence of phenylpyruvic acid. Of course, phenylpyruvic acid was to be expected since Bettzieche and

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[1] Part of the material contained in this paper was presented before the Division of Organic Chemistry at the Pittsburgh meeting of the American Chemical Society, September, 1936.

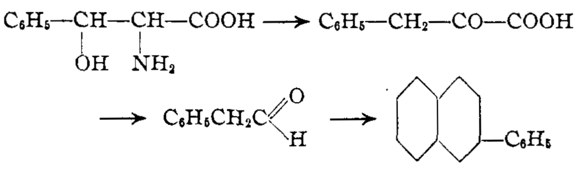
[2] Schrauth and Geller, *Ber.*, **55**, 2783 (1922).

[3] Erlenmeyer, *Ann.*, **307**, 82 (1899).

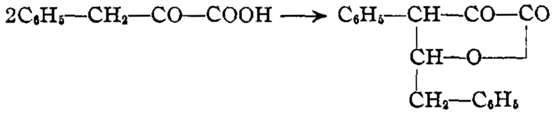
[4] Zincke and Breuer, *ibid.*, **226**, 24 (1884).

[5] Bettzieche, *Z. physiol. Chem.*, **150**, 177 (1925).

others have shown that α-amino-β-hydroxy acids tend to lose water yielding an unstable α-amino-α,β-unsaturated acid which hydrolyzes readily to an α-keto acid. On the basis of this evidence Bettzieche assumed the following mechanism for the production of β-phenylnaphthalene



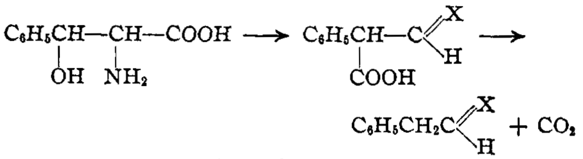
At this point, our earlier work was repeated and evidence was obtained for the formation of phenylpyruvic acid and phenylacetaldehyde from the aminomethoxy acids under the influence of hydrobromic acid. Therefore, a study was made of the action of sulfuric and hydrobromic acids on phenylpyruvic acid under various conditions. The only substance produced in detectable amounts in these reactions was α-keto-β,δ-diphenyl-γ-valerolactone.



$$2C_6H_5—CH_2—CO—COOH \longrightarrow \begin{array}{l} C_6H_5—CH—CO—CO \\ \qquad\;\; CH—O—\!\!\rfloor \\ \qquad\;\; CH_2—C_6H_5 \end{array}$$

These results eliminate phenylpyruvic acid as a possible intermediate in the formation of phenylacetaldehyde or β-phenylnaphthalene and indicate that the small amount of α-keto-β,δ-diphenyl-γ-valerolactone isolated from the aminomethoxy acid reaction product was produced by a side reaction.

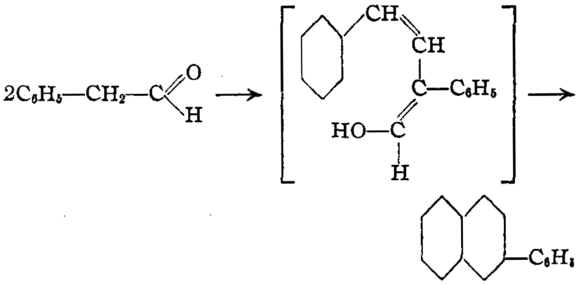
Since phenylpyruvic acid is not a precursor of either β-phenylnaphthalene or phenylacetaldehyde, the formation of these two substances must be explained in another way; and, since phenylacetaldehyde is known to yield the hydrocarbon under the conditions used, it seems very probable that phenylacetaldehyde is an intermediate in the formation of the β-phenylnaphthalene. A possible mechanism for this transformation was suggested by the fact that phenylethyleneglycol under the influence of sulfuric acid undergoes a semipinacolinic rearrangement yielding phenylacetaldehyde,[6] which, under the conditions of the rearrangement, is transformed into β-phenylnaphthalene.[4] Now phenylserine also may undergo such a rearrangement as shown in the following equations



X = O or NH

These reactions not only provide a satisfactory mechanism for the production of phenylacetaldehyde as an intermediate, but they also afford a logical explanation for the evolution of carbon dioxide during the reaction, since the product of the rearrangement, if either the phenyl or carboxyl group migrates, is an unstable β-aldehydo acid which would be decarboxylated readily. Such a rearrangement has an analogy in the conversion of ethyl phenylglycidate to ethyl formylphenylacetate,[7] and the rearrangement of 1-phenyl-1-hydroxy-2-aminopropane to phenylmethylacetaldehyde[8] on treatment with nitrous acid.

The final steps in the formation of β-phenylnaphthalene would then involve an aldol condensation of two molecules of phenylacetaldehyde followed by ring closure.



A possible objection to this formulation of the reaction is the fact that both phenylacetaldehyde and phenylethyleneglycol give a lower yield of β-phenylnaphthalene than does phenylserine. However, this discrepancy loses its significance in view of the behavior of β-phenyl-β-hydroxyethylamine—a compound which is related closely in structure to both phenylserine and phenylethyleneglycol. β-Phenyl-β-hydroxyethylamine, when refluxed with hydrobromic acid, was converted into β-phenylnaphthalene in exactly the same manner as phenylserine. This result strongly supports the semipinacolinic rearrangement postulation. Phenylglyceric acid also was studied in order to compare its behavior with that of phenylserine. In this case, the yield of the hydrocarbon

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(6) Zincke, *Ann.*, **216**, 286 (1882).

(7) Tiffeneau and Levy, *Anales asoc. quim. argentina*, **18**, 144 (1930).

(8) McKenzie, Luis and Mitchell, *Ber.*, **65**, 798 (1932).

was quite low. A comparison is hardly justified, however, since a considerable amount of the phenylglyceric acid was converted to phenylpyruvic acid. The fact that some β-phenylnaphthalene was obtained, however, also supports the view that a semipinacolinic rearrangement occurs.

These results indicate that the presence of a nitrogen atom in the molecule facilitates the reaction, perhaps by a solubilizing effect. It is possible that phenylacetaldimine is the intermediate in the case of the amino compounds. If so, the condensation reactions would occur in a moderately dilute aqueous solution, thus favoring intramolecular cyclization rather than intermolecular polymerization of the aldol condensation product.

Another possible explanation of the difference between the glycols and the amino compounds was afforded by a further study of the behavior of phenylethyleneglycol under the influence of hydrobromic acid. If all of the glycol was added to the hydrobromic acid at the beginning of the reaction, the yield of the hydrocarbon was poor and there was formed a considerable amount of tar which became more viscous with further heating. This tar must be polymerized phenylacetaldehyde. When a solution of the glycol in hydrobromic acid was added slowly to boiling hydrobromic acid, the yield of the hydrocarbon was increased greatly and the amount of tar was small. This suggests the possibility that the rearrangement of the amino compounds proceeds more slowly than that of the glycol, producing phenylacetaldehyde at a rate sufficiently slow to prevent its accumulation in the reaction mixture.

In conclusion it might be pointed out that the ease of preparation of the aminomethoxy acids and the smoothness with which they are converted into β-phenylnaphthalene make this a satisfactory preparative method for the hydrocarbon. These reactions should be applicable also in preparing other hydrocarbons from the appropriate α-amino-β-methoxy-β-arylpropionic acids.

Experimental

α-Amino-β-methoxy-β-phenylpropionic Acids.—The α-bromo-β-methoxy-β-phenylpropionic acids[9] were heated with 10 volumes of concentrated ammonium hydroxide for five hours at 80–90°. The amino acids were isolated and purified in the usual way. The yields were 45–55% of the theoretical amount. Both of the amino acids are insoluble in water. The aminomethoxy acid (IIa) (from the bromo acid melting at 183–184°) melts with decomposition at 253–254° and gives a benzoyl derivative melting at 221–222°.

Anal. Calcd. for $C_{10}H_{13}O_3N$: N, 7.18. Found: N, 7.11. Calcd. for $C_{17}H_{17}O_4N$: N, 4.68. Found: N, 4.74.

The aminomethoxy acid (IIb) (from the bromo acid melting at 139–140°) melts with decomposition at 235–238° and gives a benzoyl derivative melting at 153–154°.

Anal. Calcd. for $C_{10}H_{13}O_3N$: N, 7.18. Found: N, 7.30. Calcd. for $C_{17}H_{17}O_4N$: N, 4.68. Found: N, 4.62.

Treatment with Hydrobromic and Sulfuric Acids

1. **Aminomethoxy Acids.** **(a.)**—The aminomethoxy acids were refluxed for one hour with 20 volumes of 48% hydrobromic acid. The solution became turbid almost immediately after refluxing began. An oil soon separated and increased in amount during the course of the reaction. At the end of fifty to sixty minutes the turbidity disappeared, leaving a clear aqueous layer with a brown oil floating on the surface. The solution was cooled and poured into four volumes of cold water. The reaction product was extracted with ether and the ether solution was washed twice with water and dried. The ether was distilled, leaving a yellow crystalline solid. This material was recrystallized from 10 volumes of hot alcohol giving a light yellow solid melting at 101–103°, which was practically pure β-phenylnaphthalene. The yield was 80–85% of the theoretical amount. Colorless β-phenylnaphthalene (m. p. 103–104°) is obtained by distillation of the crude material under reduced pressure (b. p. 185–190° at 5 mm.) followed by recrystallization of the distillate from ethyl alcohol.

Anal. Calcd. for $C_{16}H_{12}$: C, 94.12; H, 5.88. Found: C, 93.70, 93.94; H, 5.72, 5.99.

In one run the original ether solution was extracted with 1 *N* sodium hydroxide solution. The extract was acidified with dilute sulfuric acid, precipitating a solid which was removed by filtration, washed with cold water, and recrystallized from hot ethyl alcohol, giving a white crystalline solid which melted at 169–171°. There was no depression of the melting point when this substance was mixed with α-keto-β,δ-diphenyl-γ-valerolactone. Only 0.3 g. of this material was obtained from 20 g. of aminomethoxy acid.

(b.)—The above experiment was repeated using a 3-necked flask equipped with a condenser set for distillation and a dropping funnel through which 48% hydrobromic acid was added to replace that lost by distillation. β-Phenylnaphthalene appeared with the first drops of distillate, indicating the rapidity with which the reaction occurs. The distillate (which had a strong odor of phenylacetaldehyde) was poured into 4 volumes of water and extracted with ether. The ether solution was washed twice with water and dried. The ether was removed and the residue was extracted with a small amount of cold alcohol. The alcohol solution was treated with semicarbazide hydrochloride and sodium acetate yielding a semicarbazone which after repeated recrystallization from ethyl alcohol melted at 151–153°. Auwers and Keil[10]

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[9] Van Loon and Carter, THIS JOURNAL, **59**, 2555 (1937).

[10] Auwers and Keil, *Ber.*, **36**, 3902 (1903).

reported that the semicarbazone of phenylacetaldehyde melts at 153°.

The yield of β-phenylnaphthalene by this procedure was 60–70% of the theoretical amount—somewhat lower than in the previous experiment.

(c).—Experiment (a) was repeated using 30, 20, and 10% sulfuric acid instead of hydrobromic acid. The refluxing was continued for twelve to fifteen hours. Ten per cent. sulfuric acid had little effect on the aminomethoxy acids although the odor of phenylacetaldehyde could be detected. Thirty and twenty per cent. sulfuric acid converted the amino acids into β-phenylnaphthalene in yields of 50 and 10%, respectively, of the theoretical amount.

2. **Phenylserine.**[11]—Experiments 1a and 1b were repeated with identical results.

3. **β-Phenyl-β-hydroxyethylamine.**[12]—Ten grams of β-phenyl-β-hydroxyethylamine was refluxed with 200 cc. of 48% hydrobromic acid. The solution became turbid almost immediately and an oil began to separate. At the end of one hour the heating was discontinued and the reaction mixture was worked up as in 1a. The yield of β-phenylnaphthalene was 5.9 g. (79% of the theoretical amount).

4. **Phenylethyleneglycol.**[13] (a.)—Ten grams of phenylethyleneglycol was refluxed with 200 cc. of 48% hydrobromic acid for one hour and the reaction product was worked up in the usual way. On attempting to recrystallize the crude material from ethyl alcohol a dark brown tar precipitated with the β-phenylnaphthalene. In later experiments the hydrocarbon was separated from the tar by two or three extractions of the crude product with hot petroleum ether in which β-phenylnaphthalene is fairly soluble. The yield was 2.7 g. (36% of the theoretical amount).

(b.)—Ten grams of phenylethyleneglycol was dissolved in 75 cc. of 48% hydrobromic acid and the solution was added to 125 cc. of boiling hydrobromic acid during twenty-five minutes. The reaction mixture was kept refluxing vigorously during the course of the addition and for thirty-five minutes after the addition was complete. The reaction product was worked up as in 4a. The yield of β-phenylnaphthalene was 5.7 g. (78% of the theoretical amount).

5. **Phenylpyruvic Acid.**[14] (a.)—Phenylpyruvic acid was refluxed with 50 volumes of sulfuric acid (10 and 30%) for twelve hours and with 20 volumes of hydrobromic acid (48%) for five hours. The only substances which could be isolated from the reaction mixtures were phenylpyruvic acid and α-keto-β,δ-diphenyl-γ-valerolactone. The yield of the latter ranged from 15% of the theoretical amount with 10% sulfuric acid to 70% of the theoretical amount with 48% hydrobromic acid. No β-phenylnaphthalene could be isolated by extraction of the crude reaction products with hot petroleum ether.

(b.)—The experiments with phenylpyruvic acid were repeated as in (a) except that the reaction mixture was distilled and solvent was added continuously through a separatory funnel to replace that lost. In the runs with sulfuric acid, water was added; in the runs with hydrobromic acid, 48% hydrobromic acid. None of the distillates contained phenylacetaldehyde or β-phenylnaphthalene. The hydrobromic acid distillate contained a small amount of phenylpyruvic acid. The yields of α-keto-β,δ-diphenyl-γ-valerolactone in these experiments were the same as in (a).

Summary

1. The α-amino-β-methoxy-β-phenylpropionic acids, phenylserine, β-phenyl-β-hydroxyethylamine, phenylethyleneglycol, and phenylglyceric acid are converted into β-phenylnaphthalene when refluxed with hydrobromic acid.

2. Phenylpyruvic acid is converted into α-keto-β,δ-diphenyl-γ-valerolactone when refluxed with hydrobromic acid.

3. The mechanism of formation of β-phenylnaphthalene is discussed.

URBANA, ILLINOIS

RECEIVED FEBRUARY 4, 1938

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[11] Erlenmeyer and Früstück, *Ann.*, **284**, 36 (1894).

[12] Read and Campbell, *J. Chem. Soc.*, 2682 (1930).

[13] Evans and Morgan, THIS JOURNAL, **35**, 54 (1913).

[14] Erlenmeyer and Arbenz, *Ann.*, **333**, 229 (1904).