Table II gives a few typical experiments performed with a mercury cathode and a smooth platinum anode, of approximately the same area as the carbon anode used in the previous experiments. Apparently as shown by experiment 93, aqueous sulfuric acid in this concentration is not a desirable electrolyte for this reduction. However, there is a possibility that other cathode potentials and other sulfuric acid concentrations may yield the pinacol. An aqueous alcohol acid solution will, by some mechanism, yield larger quantities of *p*-aminoacetophenone hydrol than an aqueous acid solution. Another observation is that, under conditions of experiments 95 and 96, 97 and 98, relatively higher temperatures favor hydrol, rather than pinacol formation. Also from 97 and 98, it can be seen that −2.6 volts cathode potential is too high for the satisfactory formation of pinacol.

Acknowledgment.—We wish to thank Joseph A. Walter for the construction of the apparatus and Jerry C. Cavagnol, Robert W. Wynn and John F. Yost for their helpful contributions to the development of the electrolytic reduction apparatus. We also wish to thank the Microanalytical Laboratory of the National Institutes of Health for the microanalyses.

Summary

An electrolytic reduction method has been developed for the preparation of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol which gives satisfactory yields. It has been shown that the formation of this pinacol is dependent on the cathode potential, temperature, concentration of ketone and acid, and is somewhat independent of the current density and applied voltage. Therefore, more stress should be placed on cathode potential than on current density or applied voltages which are not constants in the electrolytic reduction process.

BALTIMORE 18, MD. RECEIVED OCTOBER 18, 1948

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

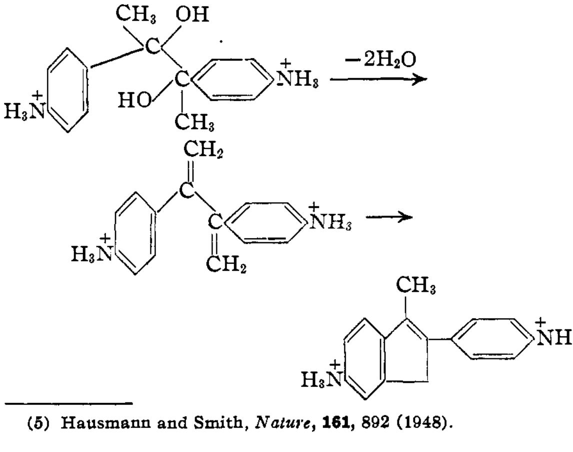
Chemical Studies on Pinacols Obtained from *p*-Aminoacetophenone and *p*-Aminopropiophenone[1]

BY MILTON J. ALLEN[2] AND ALSOPH H. CORWIN*

This study was undertaken primarily to develop a method for the synthesis of α,β-dialkyl-4,4'-stilbenediamines. A method has been reported[3] for the preparation of α,β-diethyl-4,4'-stilbenediamine by the conversion of α,β-diethyl-4,4'dibromostilbene to the desired diamine. However, the preparation of the intermediates appeared laborious, and, therefore, a simpler method was developed. Previous work has shown[4] that α,β-diethyl-4,4'-stilbenediol could be prepared by use of the pinacol–pinacolone and retro-pinacol rearrangements. This general scheme was followed with some very interesting side reactions.

The rearrangement of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol dihydrochloride (I), which was accomplished by refluxing the compound with a 1:2 ratio by volume of concentrated hydrochloric acid to water, yielded two products, a ketone (III) and a compound which had a molecular formula of $C_{16}H_{18}N_2Cl_2$ (II). The last compound was presumed to be either a butadiene or an indene. If the compound possessed a butadiene structure and reduction with sodium and alcohol proceeded predominantly one-four, the resulting compound would be a substituted stilbene. This compound in turn would be readily reduced to the saturated compound under the conditions of the experiment because of the presence of a conjugated system. Therefore, the first possibility was eliminated, for as a result of reduction, a compound $C_{16}H_{18}N_2$ (IIA) was obtained.

A butadiene type structure may be intermediate in the formation of the indene. Recently Hausmann and Smith[5] demonstrated that treatment of dienestrol with $1N$ mineral acids gave 1-methyl-2-(*p*-hydroxyphenyl)-3-ethyl-6-hydroxyindene. On the basis of this experimental evidence we may propose the following mechanism for the formation of the aminoindene.



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* Harvard University Ph.D. 1932.

[1] This investigation was supported (in part) by a research grant awarded to M. J. A., by the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

[2] (a) Research Fellow, National Cancer Institute 1947–1949; (b) from the Ph.D. dissertation of Milton J. Allen, The Johns Hopkins University, June, 1949.

[3] Vargha and Kovacs, *Ber.*, **75**, 794 (1942).

[4] Wessely, *et al.*, *Monatsh.*, **73**, 127 (1940).

[5] Hausmann and Smith, *Nature*, **161**, 892 (1948).

Orechoff and Tiffeneau[6] showed that when 1,2,3-triphenylpropanediol was dehydrated, 1,2-diphenylindene was obtained. Probably as a result of this work Bergmann[7] became interested in the investigations of Johlin[8] and Lucas and Legagneur[9] and proved that the $C_{16}H_{14}$ compound obtained by dehydration of acetophenone pinacol, was not 2,3-diphenylbutadiene or 9,10-dimethylanthracene as was suspected, but 2-phenyl-3-methylindene. Both of these investigations form strict structural analogies for the formation of the aminoindene from 2,3-bis-(*p*-aminophenyl)-2,3-butanediol.

The fact that acetophenone pinacol does not form an indene under conditions similar to those which will give the amino indene probably indicates that the $-\overset{+}{N}H_3$ groups activate the molecule in such a way, in the presence of added acid, that the rate of indene formation increases and the rate of ketone formation decreases.

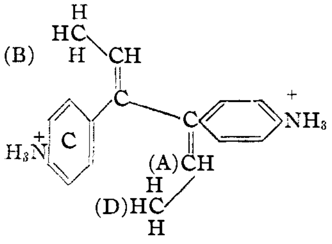
Refluxing the dihydrochloride of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol in aqueous solution or allowing such a solution to stand at room temperature for a period of time it was possible to isolate only ketone. The ketone (III) 1,2-(di-*p*-aminophenyl)-2-methylpropanone-1 dihydrochloride, upon reduction gave the alcohol (IV). This, when treated with acid, underwent the retro-pinacol rearrangement to give the α,β-dimethyl-4,4'-stilbenediamine. This structure was established by deamination and isolation of a compound identified as *trans*-α,β-dimethylstilbene.

The pinacol of *p*-aminoacetophenone upon rearrangement forms compound III, as a result of migration of the methyl group. The ketone structure was established by two reactions. First a negative iodoform test was obtained and second, upon methylation and subsequent alkali fission of the methylated ketone, *p*-dimethylaminobenzoic acid was obtained. If this compound had been a methyl ketone, or a mixture of ketones, acetic acid would have been one of the reaction products. This was not found to be the case and therefore in view of the fact that free base of this ketone, obtained in quantitative yield from the dihydrochloride, had a sharp melting point it can be assumed that the ketone structure is as shown.

This shift of methyl group is not inconsistent with previous work on symmetrical pinacols. The work of Bachmann and Sternberger[10] and Price and Mueller[11] shows that the strongest electron donating group migrates. In our case the strongest electron donating group is the methyl group. This is the group that is observed to migrate.

3,4-Bis-(*p*-aminophenyl)-3,4-hexanediol dihydrochloride (VI) when subjected to treatment with varying concentrations of hydrochloric acid gave results similar to that obtained with 2,3-bis-(*p*-aminophenyl)-2,3-butanediol dihydrochloride. Refluxing with a more concentrated aqueous solution of acid resulted in the formation of the ketone (VII), 1,2-(di-*p*-aminophenyl)-2-ethylbutanone-1 dihydrochloride and the indene (VIII) which according to the proposed mechanism should be 1-methyl-2-(*p*-aminophenyl)-3-ethyl-6-aminoindene dihydrochloride. A more dilute acid solution yielded only the ketone (VII).

It is interesting to note that the yield of this indene was only 10.3% as compared to a 60.7% yield of the indene from 2,3-bis-(*p*-aminophenyl)-2,3-butanediol. Electronically, the methyl groups B and D in (VIA) should favor ring closure. The fact that a diminished yield is observed instead can reasonably be ascribed to a steric factor.



VI A

With most orientations of the atoms in compound VIA the hydrogens of groups B and D collide with the hydrogens of ring C while the molecule is in the process of rotation for ring closure between carbon A and ring C. This steric interference would tend to diminish the probability of formation of the ideal form for ring closure from the average form of the molecule.

An indane (VIIIA) was obtained upon reduction of the indene. The ketone (VII) upon reduction with sodium and alcohol and subsequent treatment with a 50% volume solution of hydrochloric acid yielded α,β-diethyl-4,4'-stilbenediamine.

Experimental[12]

2-(*p*-Aminophenyl)-3-methyl-6-aminoindene Dihydrochloride (II).—In a one-liter round-bottomed flask 28.6 g. of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol dihydrochloride[13] was dissolved in a solution of 100 ml. of concentrated hydrochloric acid and 200 ml. of water and refluxed for one and one-half hours. After the addition of 100 ml. of concentrated hydrochloric acid, the reaction mixture was chilled overnight. The crystals of the indene were filtered and washed lightly with a 50% by volume aqueous hydrochloric acid solution. The crystals can be further purified by dissolving in a minimum amount of water and precipitating by the addition of an equal volume of hydrochloric acid; yield 16.2 g. (60.7%). This compound decomposes at about 250°.

Anal. Calcd. for $C_{16}H_{18}N_2Cl_2$: C, 62.13; H, 5.86; N, 9.06; Cl, 22.93. Found: C, 62.16; H, 5.85; N, 9.01; Cl, 22.91.

The free base was prepared and recrystallized from methanol; m. p. 168–169° (dec.).

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[6] Orechoff and Tiffeneau, *Bull. soc. chim.*, [4] **31**, 253 (1922).

[7] Bergmann, *Ber.*, **65B**, 109 (1932).

[8] Johlin, THIS JOURNAL, **39**, 292 (1917).

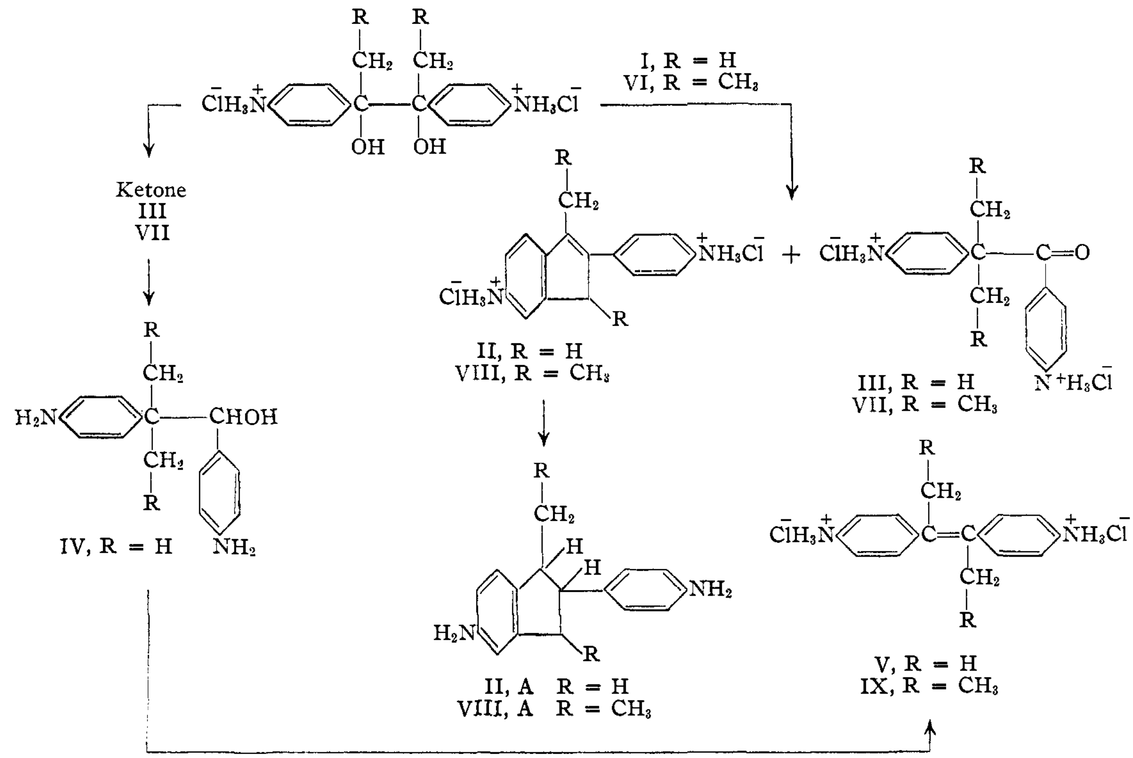
[9] Lucas and Legagneur, *Bull. soc. chim.*, [4] **45**, 718 (1929).

[10] Bachmann and Sternberger, THIS JOURNAL, **56**, 170 (1934).

[11] Price and Mueller, *ibid.*, **66**, 634 (1944).

[12] All melting points are uncorrected.

[13] Allen and Corwin, THIS JOURNAL, **72**, 114 (1950).



Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.31; H, 6.82. Found: C, 81.41; H, 7.09.

Attempts to deaminate this compound was unsuccessful as the resulting products were apparently polymeric substances. Increasing or decreasing the quantity of acid did not improve the yields of the indene. Increased acid concentrations caused decomposition with lower over-all yields of the indene and ketone, while lower acid concentrations gave lower yields of the indene and larger yields of the ketone.

Additional indications for the indene structure was the red color obtained with cold concentrated sulfuric acid,[14] and a dark red precipitate with antimony pentachloride.[15]

The acid mother liquor was evaporated to a small volume and placed in the refrigerator overnight. The crystals were filtered and washed lightly with cold absolute ethanol: yield of ketone III, 8.35 g. (29.6%); m. p. 272–275° (dec.).

Anal. Calcd. for $C_{16}H_{20}N_2OCl_2$: C, 58.71; H, 6.16; N, 8.56. Found: C, 58.83; H, 6.37; N, 8.38.

The free base was prepared by dissolving the dihydrochloride in water and making the solution alkaline. An oil formed and after washing a number of times with water was triturated with water to yield a white powder. Upon crystallization from water the free base in quantitative yield was obtained; m. p. 137.5–138°.

Anal. Calcd. for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13. Found: C, 75.69; H, 7.07.

2-(*p*-Aminophenyl)-3-methyl-6-aminoindane (IIA).—A mixture of 1.2 g. of the above indene dihydrochloride and 60 ml. of anhydrous *n*-propyl alcohol was heated to reflux. Over a one-hour period, 3.6 g. of sodium was added portionwise. The mixture was allowed to reflux an additional hour and then an equal volume of water was added and the propyl alcohol removed under vacuum.

The crystalline mass was removed by filtration, and after recrystallization from methanol, white crystals were obtained: yield 0.83 g. (92.5%); m. p. 162–163° (dec.).

Anal. Calcd. for butane structure $C_{16}H_{20}N_2$: C, 79.95; H, 8.38; N, 11.66. Calcd. for indane structure $C_{16}H_{18}N_2$: C, 80.62; H, 7.61; N, 11.75. Found: C, 80.54; H, 7.70; N, 11.67.

Deamination of this compound yielded an oil which could not be crystallized and as the deaminated product was not described in the literature positive identification could not be made by this means.

The dihydrochloride was prepared by dissolving the free base in a small volume of dilute hydrochloric acid and precipitating with an excess of concentrated hydrochloric acid; m. p. 310–312° (dec.).

Anal. Calcd. for $C_{16}H_{20}N_2Cl_2$: C, 61.70; H, 6.47; N, 9.03. Found: C, 61.42; H, 6.72; N, 8.88.

1,2-(Di-*p*-aminophenyl)-2-methylpropanone-1 Dihydrochloride (III).—Two grams of 2,3-bis-(*p*-aminophenyl)-2,3-butanediol dihydrochloride was dissolved in 25 ml. of distilled water and allowed to stand at room temperature for two weeks. The solution was vacuum distilled to a very small volume, a quantity of absolute ethanol added, and put in the refrigerator overnight. The crystals were filtered and washed lightly with cold absolute ethanol: yield 1.17 g. (61.7%); m. p. 272–275° (dec.).

Anal. Calcd. for $C_{16}H_{20}N_2OCl_2$: N, 8.56. Found: N, 8.42.

The free base was prepared: m. p. 137.5–138°.

An alternate method was to dissolve 2 g. of the pinacol dihydrochloride in 25 ml. of distilled water and allow to reflux for approximately eight hours. The ketone was isolated as above: yield 1.28 g. (67.5%); m. p. 272–275° (dec.).

Anal. Calcd. for $C_{16}H_{20}N_2OCl_2$: N, 8.56. Found: N, 8.61.

Free base m. p. 137.5–138°.

Fission of Ketone III.—One gram of the ketone dihydrochloride was dissolved in 25 ml. of 76% ethanol to which was added 1.7 g. of potassium carbonate dissolved in 10 ml. of water, and then 1.2 ml. of dimethyl sulfate added. The mixture was refluxed for two hours, an excess of water added and the mixture extracted a number of

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[14] Spiker and Dombrowsky, *Ber.*, **42**, 573 (1909).

[15] Hilpert and Wolf, *ibid.*, **46**, 2215 (1913).

times with ether. The ether was dried and evaporated. The residue was treated with benzenesulfonyl chloride in the presence of 10% sodium hydroxide and the tertiary amine separated in the usual manner. A low yield was obtained in this reaction. The tertiary amine was dissolved in 50 ml. of absolute ethanol to which was added 3 g. of potassium hydroxide. The reaction mixture was allowed to reflux for ten days in a nitrogen atmosphere. At the end of this period the alcohol was evaporated, the residue taken up in water and extracted several times with ether. The aqueous solution was made slightly acid with hydrochloric acid, the precipitate collected and recrystallized twice from ethanol; m. p. 234–236°. A satisfactory yield of product was obtained based on the tertiary amine. The reported values for *p*-dimethylaminobenzoic acid[16] vary from 234–240°. One worker[17] reported a value of 235°. The mother liquor obtained after removal of the *p*-dimethylaminobenzoic acid was saturated with sodium chloride and extracted a number of times with ether. The ether was evaporated and no acetic acid was found in the residue.

1,2-(Di-*p*-aminophenyl)-2-methylpropanol-1 Dihydrochloride (IV).—Five grams of the ketone dihydrochloride was suspended in 85 ml. of anhydrous *n*-propyl alcohol and heated to reflux. Five and one-half grams of sodium was added in portions over a period of one and one-half hours. The mixture was allowed to reflux an additional hour, an excess of water added and the propyl alcohol evaporated. After chilling, the water was decanted from the gummy residue and the residue washed a number of times with water. The dried residue was dissolved in a minimum amount of absolute ethanol, filtered, and evaporated to a small volume. To the chilled solution was added cold concentrated hydrochloric acid and the remainder of the ethanol removed under vacuum. The resulting solution was refrigerated overnight, the crystals collected and washed with a solution of equal parts of anhydrous ethanol and ethyl acetate: yield 4.1 g. (81.5%); m. p. 309–311° (dec.).

Anal. Calcd. for $C_{16}H_{22}N_2OCl_2$: C, 58.36; H, 6.73; N, 8.51. Found: C, 58.29; H, 6.81; N, 8.39.

α,β-Dimethyl-4,4′-stilbenediamine (V).—A solution of 4.1 g. of the hydrol IV, 50 ml. of water and 50 ml. of concentrated hydrochloric acid was refluxed for two hours. About thirty minutes after refluxing was started, crystals appeared, and their quantity increased as the refluxing was continued. The reaction mixture was placed in the refrigerator overnight and then filtered. The collected crystals were washed lightly with cold absolute ethanol: yield 2.9 g. (74.8%); m. p. 330–332° (dec.).

The free base was prepared and recrystallized from 60% methanol with an excellent yield; m. p. 145–146° (dec.).

Anal. Calcd. for $C_{16}H_{18}N_2$: C, 80.62; H, 7.61; N, 11.75. Found: C, 80.66; H, 7.60; N, 11.65.

It is not necessary to isolate the hydrol before a retropinacol rearrangement. Instead, after reduction, two volumes of water and one volume of hydrochloric acid are added and then distilled at atmospheric pressure to a small volume and placed in the refrigerator overnight to crystallize. This will result in a 75% yield of the α,β-dimethyl-4,4′-stilbenediamine dihydrochloride based on the ketone.

Deamination of Compound V.—One gram of the stilbene dihydrochloride was dissolved in 60 ml. of water to which was added 4 ml. of concentrated hydrochloric acid. The solution was chilled to 0°, and an aqueous solution containing 0.52 g. of sodium nitrite (97.5%) was added. After allowing the solution to stand at 0° for fifteen minutes, 24 ml. of 30% hypophosphorous acid was added, and the flask loosely stoppered and placed in the refrigerator for thirty-six hours. The mixture was extracted a few times with benzene and the combined extracts washed with dilute sodium hydroxide solution and water. After drying over anhydrous potassium carbonate, the benzene was evaporated. The residue was crystallized from methanol. Recrystallization from methanol yielded a compound melting at 103–105°. The reported value[18] for *trans*-α,β-dimethylstilbene is 107°.

Attempted Preparation of 2-Phenyl-3-methylindene.—One-half gram of acetophenone pinacol was refluxed for two hours with a solution consisting of 25 ml. of concentrated hydrochloric acid and 25 ml. of water. The desired indene was not found in the reaction products. Refluxing and identical reaction mixture for twenty-four hours also yielded negative results.

3,4-bis-(*p*-Aminophenyl)-3,4-hexanediol (VI).—The apparatus used for the preparation of this compound was the same as used previously. A solution of 106.4 g. of *p*-aminopropiophenone[19] in 700 ml. of 10% by volume of hydrochloric acid was placed in the cathode chamber of the electrolysis cell. At a cathode potential of −1.5 v. compared to a saturated calomel half-cell, the initial current was 2.55 amp. According to calculations for a one electron change per molecule of ketone, the reduction should take seven and one-half hours. During the course of the reduction, the temperature was kept at about 28°. At the end of the calculated period, the current had decreased and the hydrogen gas was being evolved from the cathode surface. A light yellow crystalline product was obtained in the same manner as previously described[13]; yield 76.5 g. (57.4%). More negative cathode potentials did not result in better yields. The compound decomposed at about 202°.

The free base was prepared and upon recrystallization from 95% ethanol, a good yield of crystalline product was obtained; m. p. 205–206° (dec.).

Anal. Calcd. for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 72.10; H, 8.26; N, 9.28.

1,2-(Di-*p*-aminophenyl)-2-ethylbutanone-1 Dihydrochloride (VII) and 1-Methyl-2-(*p*-aminophenyl)-3-ethyl-6-aminoindene Dihydrochloride (VIII).—Ten grams of 3,4-bis-(*p*-aminophenyl)-3,4-hexanediol dihydrochloride was dissolved in 100 ml. of water to which was then added 50 ml. of concentrated hydrochloric acid. The solution was treated in a manner similar to that previously discussed and the indene isolated was washed with a 30% solution of absolute ethanol in ethyl acetate; yield 0.95 g. (10.3%). This product decomposes at about 220°. It gave a fuchsin red color with cold concentrated sulfuric acid[14] and a dark red precipitate with a carbon tetrachloride solution of antimony pentachloride.[15]

Anal. Calcd. for $C_{18}H_{22}N_2Cl_2$: C, 64.10; H, 6.57; N, 8.30; Cl, 21.02. Found: C, 64.18; H, 6.51; N, 8.19; Cl, 21.08.

The ketone was isolated from the acid mother liquor and washed with a 20% solution of absolute ethanol in ethyl acetate: yield 6.5 g. (68.4%); m. p. 235–237° (dec.).

The free base was prepared in over 90% yield by recrystallization from 60% methanol; m. p. 120.5–121°.

Anal. Calcd. for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.59; H, 7.95; N, 10.24.

The ketone was also prepared by dissolving 4 g. of the pinacol dihydrochloride in 50 ml. of water to which 14.5 ml. of concentrated hydrochloric acid had been added and allowed to reflux for one and one-half hours. The solution was worked up in the same manner as the previous acid mother liquor: yield 3.36 g. (88.3%); m. p. 235–237° (dec.); free base m. p. 120.5–121°.

α,β-Diethyl-4,4′-diaminostilbene (IX).—One-half gram of the ketone was added to 10 ml. of anhydrous *n*-propyl alcohol. To the refluxing mixture was added 0.6 g. of sodium in small portions over a period of twenty minutes. The reaction mixture was allowed to reflux for an additional hour, 100 ml. of water added, most of the alcohol evaporated and the resulting mixture placed in the refrigerator overnight. The hydrol was filtered, washed with water and dissolved in 6 ml. of concentrated hydrochloric acid and 6 ml. of water. The solution was refluxed for three hours, chilled and the crystals filtered. The crystalline dihydrochloride was washed with a 50% solution of absolute ethanol in ethyl acetate. It was pos-

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[16] "Beilstein," **14**, p. 427.

[17] Michler, *Ber.*, **9**, 400 (1876).

[18] Ott, *Ber.*, **61**, 2119 (1928).

[19] Purchased from the Eastman Kodak Company.

sible to obtain an additional crop of crystals from the mother liquor by evaporation to a smaller volume, yield 0.38 g. (80.2%), decomposes at about 230°.

The free base was prepared and recrystallized from methanol with almost quantitative yield; m. p. 131-132°. This agrees with the melting point reported in the literature.[3]

1-Methyl-2-(*p*-aminophenyl)-3-ethyl-6-aminoindane Dihydrochloride (VIIIA).—One-half gram of the indene was reduced in the same manner as was the above ketone. After chilling overnight, the aqueous portion was decanted and the residue washed a number of times with water. The residue was taken up in a small quantity of absolute ethanol to which was added 1 ml. of concentrated hydrochloric acid. The alcohol was evaporated and the acid solution chilled overnight. The crystals were filtered and washed with a 20% solution of absolute ethanol in ethyl acetate; yield 0.42 g. (84.5%); m. p. 280-283° (dec.).

Anal. Calcd. for $C_{18}H_{24}N_2Cl_2$: C, 63.71; H, 7.13; N, 8.25. Found: C, 63.82; H, 7.23; N, 8.22.

Acknowledgment.—We wish to thank the Microanalytical Laboratory of the National Institutes of Health and Mr. Ervin Pritchett of this department for the microanalyses.

Summary

A method has been developed for the preparation of α,β-dimethyl- and α,β-diethyl-4,4′-stilbenediamine by a pinacol–pinacolone type rearrangement of the respective pinacol. Reduction of the ketone formed with subsequent retro-pinacol rearrangement and dehydration gave the desired stilbene.

The 3,4-bis-(*p*-aminophenyl)-3,4-hexanediol was prepared by bimolecular electrolytic reduction.

In the rearrangement of the pinacols it was found that varying concentrations of acid would yield either the ketone exclusively or a mixture of ketone and substituted 6-aminoindene.

It has also been shown that apparently the presence of the $-\overset{+}{N}H_3$ under conditions of the experiment will activate the molecule so it will undergo ring closure more readily than when a phenyl group alone is present.

BALTIMORE 18, MARYLAND RECEIVED OCTOBER 18, 1948

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE RADIATION LABORATORY OF THE UNIVERSITY OF CALIFORNIA, BERKELEY]

The Mechanism of the Willgerodt Reaction[1]

BY W. G. DAUBEN,* J. C. REID,[2] P. E. YANKWICH[3] AND M. CALVIN

The question as to whether the Willgerodt reaction[4] involves a rearrangement of the molecule when a ketone is converted to a carboxylic acid of the same number of carbon atoms has been the subject of wide investigation.[5] Willgerodt[5] originally postulated that the reaction did not involve a rearrangement of the carbon skeleton of the molecule while later the work of Fieser and Kilmer[5] tended to cast doubt on the validity of his proof. Kinkler and Li,[5] on the other hand, proposed an elaborate mechanism for this reaction which involved a molecular rearrangement. Recently, Carmack and DeTar[5] and King and McMillan[5] have re-examined the original evidence of Willgerodt and have concluded that no migration of groups occurs in the reaction. The most conclusive proof, however, was offered by Shantz and Rittenberg[6] who showed that when acetophenone labeled in the carbonyl group with C^{13} was converted to phenylacetic acid, the carboxyl group of the acid contained no excess over normal of C^{13}. At the same time, the authors of the present paper reported similar results.[1] In addition, it was stated that the acidic product of the reaction appeared to be formed, in part, by an actual migration of the phenyl group. The complete results of our work are summarized in Chart I.[7]

Phenylmagnesium bromide was carbonated with radioactive carbon dioxide following the procedure described in a previous publication[8] and benzoic acid (I) was obtained in a yield of 85%. The acid was converted to benzoyl chloride with thionyl chloride. Two procedures were investigated for the preparation of acetophenone (II). In one case, the acid chloride was allowed to react with the sodium derivative of diethylmalonate and the resulting diethyl benzoylmalonate hydrolyzed and decarboxylated to the ketone[9] in an over-all yield of 78%. In the other case, benzoyl chloride was allowed to react with an excess of dimethylcadmium[10] and acetophenone was obtained in 85% yield. The Willgerodt reaction was conducted following the procedure described by Carmack and DeTar,[5] using sulfur, ammonium hydroxide and pyridine. The main product (62%) was phenylacetamide (IIIa)

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* Harvard University Ph.D. 1944.

(1) A preliminary announcement of this work was reported in a Communication to the Editor, THIS JOURNAL, **68**, 2117 (1946).

(2) Present address: National Cancer Institute, Bethesda, Maryland.

(3) Present address: Department of Chemistry, University of Illinois, Urbana, Illinois.

(4) An excellent review of this reaction is to be found in "Organic Reactions," Volume III, John Wiley and Sons, Inc., New York, N. Y., 1946.

(5) Willgerodt and Merk, *J. prakt. Chem.*, [2] **80**, 192 (1909); Fieser and Kilmer, THIS JOURNAL, **62**, 1354 (1940); Kindler and Li, *Ber.*, **74**, 321 (1941); Carmack and DeTar, THIS JOURNAL, **68**, 2029 (1946); King and McMillan, *ibid.*, **68**, 632 (1946).

(6) Shantz and Rittenberg, THIS JOURNAL, **68**, 2109 (1946).

(7) The asterisk denotes the labeled carbon atom and the percentage is that of the *initial specific activity* found in that carbon.

(8) Dauben, Reid and Yankwich, *Anal. Chem.*, **19**, 828 (1947).

(9) Wilds and Beck, THIS JOURNAL, **66**, 1688 (1944).

(10) Gilman and Nelson, *Rec. trav. chim.*, **55**, 518 (1936); Cason, THIS JOURNAL, **68**, 2078 (1946).