crystalline material, which melts at 87.2° (corr.). Artmann reports 91–92°; Fichter, 88°; Willgerodt and Heusner, 85°; and Wheeler and Liddle, 90–91°.

Compounds of 5-iodo-*o*-toluidine and 5-iodo-*o*-toluene, given in the tables, were prepared by the interaction of molecular proportions of the halogenated base and suitable reagents. It is interesting to know that the hydriodide of the base decomposed suddenly, with blackening, at 105°, in about two minutes at 100°, in 11 minutes at 90°, in 40 minutes at 80°, and in two hours at 70°. This may account for the low yields obtained when the base hydriodide was allowed to form in the reaction.

Summary

A quantitative method for the preparation of 5-iodo-2-aminotoluene (5-iodo-*o*-toluidine) has been devised.

The following derivatives of 5-iodo-*o*-toluidine were prepared and analyzed: hydrochloride, hydrobromide, hydrofluoride, hydriodide, perchlorate, picrate, picrolonate, mercurichloride, oxalate, urea, urea hydrochoride, phenylurea, α-naphthylurea, and isocyanide.

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

PLATINUM OXIDE AS A CATALYST IN THE REDUCTION OF ORGANIC COMPOUNDS. X. REDUCTION OF AMINOPHENOLS TO CYCLIC AMINO-ALCOHOLS[1]

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The desire to obtain certain cyclic amino alcohols for use in the preparation of new local anesthetics has led us to a study of the catalytic reduction of certain aminophenols. These reductions are also of interest in connection with the work on the effect of metallic salts on platinum black as a catalyst in the reduction of various organic compounds. Aldehydes could not be reduced readily with pure platinum black but reduction occurred very readily with the latter in the presence of certain salts, es-

[1] For previous articles in this field, see (a) Voorhees with Adams, THIS JOURNAL, **44**, 1397 (1922); (b) Carothers with Adams, *ibid.*, **46**, 1071 (1923); (c) Adams and Shriner, *ibid.*, **45**, 2171 (1923) (preparation of catalyst); (d) Kaufmann with Adams, *ibid.*, **45**, 3029 (1923); (e) Carothers with Adams, *ibid.*, **46**, 1675 (1924); (f) Shriner with Adams, *ibid.*, **46**, 1684 (1924); (g) Carothers with Adams, *ibid.*, **47**, 1047 (1925); (h) Pierce with Adams, *ibid.*, **47**, 1098 (1925); (i) Kern, Shriner with Adams, *ibid.*, **47**, 1147 (1925).

[2] This communication is an abstract of a portion of a thesis submitted by Hermann Heckel in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

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pecially those of iron;[1b,1e,1g] if the ease of oxidation of the substance to be reduced is associated in any way with the use of impurities to activate the platinum, the pure platinum black ought not to be so effective a catalyst for the reduction of aminophenols as platinum black in the presence of impurities.

Skita and Rolfes[3] have studied the reduction of *o*-, *m*- and *p*-aminophenol hydrochlorides in glacial acetic acid using colloidal platinum as a catalyst. The sole products, except in the case of *o*-aminophenol, were cyclohexylamine and dicyclohexylamine, the same substances that were obtained by the reduction of aniline itself.[4] The reduction has obviously not stopped with the amino alcohol but has proceeded until 4 molecular equivalents of hydrogen were absorbed. In the case of the *ortho* compound a small amount of by-product, dodecahydrophenoxazine, a condensation product of two molecules of hexahydro-*o*-aminophenol was isolated. Senderens and Aboulenc[5] using nickel as the catalyst report the reduction of *o*- and *p*-aminophenol hydrochlorides in alcoholic solution at a temperature of 180° and a pressure of 8.6 atmospheres. The corresponding amino-alcohols were obtained but no yields were given nor were any by-products mentioned.

The catalyst used in the reductions described in this investigation was platinum-oxide platinum black; the aminophenols were converted to their hydrochlorides and reduced in aqueous solution at room temperature under 2 to 3 atmospheres' pressure. The reductions were run until no more hydrogen was absorbed. The platinum oxide was made as previously described, by fusing chloroplatinic acid with sodium nitrate.[1c] Two grades of sodium nitrate, C.P. and Merck's U.S.P., were used in preparing different samples of platinum oxide, but only very pure platinum salt was employed in all cases. In every experiment comparison showed that the platinum catalyst made from Merck's U.S.P. nitrate was superior to the other. A comparison of the times of reduction is given in Table I.

TABLE I

COMPARISON OF PLATINUM CATALYST MADE FROM C. P. AND V. S. P. SODIUM NITRATE IN THE REDUCTION OF AMINOPHENOLS

Substance as hydrochloride (0.115 mole)	Time in hrs. for absorption of 3 moles of H_2 C. P. $NaNO_3$ PtO_2H_2O 0.75 g.	U. S. P. $NaNO_3$ PtO_2H_2O 0.75 g.
p-Dimethylaminophenol	30% in 18	24
m-Diethylaminophenol	18	14
m-Dimethylaminophenol	3.6	3
p-Methylaminophenol	21	9
m-Aminophenol	64% in 20	20

[3] Skita and Rolfes, *Ber.*, **53**, 1242 (1920).

[4] Skita and Berendt, *Ber.*, **52**, 1519 (1919).

[5] Senderens and Aboulenc, *Compt. rend.*, **177**, 158 (1923).

It is seen that certain of the compounds could not even be reduced to completion by the use of the C.P. sodium-nitrate platinum oxide. The impurities present in Merck's U.S.P. sodium nitrate are chiefly traces of iron and sulfate but the addition of ferrous or ferric salts to the C.P. sodium nitrate before fusing with chloroplatinic acid, did not render the catalyst formed as active as when U.S.P. sodium nitrate was used. Similar results were obtained upon addition of sulfate in the form of the acid. Addition of ferrous or ferric salts to the reduction mixture when using platinum formed by C.P. sodium nitrate fusion had no accelerating effect, in fact, if any, a slight detrimental effect on the speed of reduction. The indications are, therefore, that a minute trace of some impurity not yet determined is rendering the platinum catalyst especially active for these reductions, and emphasizes once more the important role played by traces of impurities in the catalyst in reductions.

When aldehydes were reduced oxygen could be used to reactivate the catalyst. In the reduction of aminophenols, oxygen does not exert any such influence on a spent catalyst.

The products of reduction of the *m*- and *p*-di-alkylaminophenols were mixtures of cyclohexyl-dialkyl-amine, hexahydro-dialkyl-aminophenols and a trace of cyclohexane. In the case of the *para* compound, *cis* and *trans* isomeric forms of the amino-alcohols were obtained. These could not be fractionated as they boiled at practically the same point, but the benzoate and *p*-nitrobenzoate hydrochlorides could be readily fractionally crystallized and purified. In the reduction of the *meta* compounds only one isomeric amino-alcohol was produced, or at least the isomer was present in such predominating proportions that the second modification could not be isolated. The *p*-methylaminophenol gave analogous products, cyclohexylmethylamine and hexahydro-*p*-methylaminophenol. This latter product was probably a mixture of *cis* and *trans* isomers, as concluded from the fact that when converted to the hydrochloride it melted over a wide range. No attempt was made at their separation by means of the benzoate or *p*-nitrobenzoate hydrochlorides.

The reduction of *o*- and *p*-aminophenol and *o*-dimethylaminophenol hydrochlorides presented more difficulty. It was possible to reduce the *p*-aminophenol and *o*-dimethylaminophenol only to the extent of about 25% before the platinum catalyst became inactive, the latter in particular causing the precipitation of the catalyst, no doubt due to the formation of a rather large amount of cyclohexane. The *o*-aminophenol caused an immediate poisoning of the catalyst. Whether the cause for the unsatisfactory reduction of *o*- and *p*-aminophenol is a lack of sufficient purity of the raw material has not yet been determined. The *m*-aminophenol was readily reduced with the formation of cyclohexylamine, dicyclohexylamine and *m*-cyclohexylamino-cyclohexanol, the first two sub-

stances being the same as those found by Skita in his reductions with colloidal platinum. It is interesting to note that in most of the reductions, the amount of hydrogen absorbed before reduction stopped was 3 moles, even though mixtures of products resulted.

The conclusion may be drawn that the presence of alkyl groups on the nitrogen in aminophenols has a tendency to increase the stability of the amino-alcohols formed from them.

Experimental Part

Platinum Oxide.—The details for the preparation of the platinum oxide were those described in the paper by Adams and Shriner.[1c] The chloroplatinic acid was material that had been purified according to the procedure of Wichers[6] and was fused with either Merck's C.P. or Merck's U.S.P. sodium nitrate.

Purification of Substances to be Reduced.—The alkylaminophenols were obtained from the commercial salts by treatment with alkali and extraction with benzene or ether. The solvent was then evaporated and the base distilled in a vacuum with a fractionating column. The boiling points of the fractions collected for the various amines are as follows: *p*-dimethylaminophenol, 127–128° at 4–5 mm. or 158–159° at 19–20 mm.; *m*-diethylaminophenol, 174–175° at 20 mm.; *m*-dimethylaminophenol, 152–153° at 15 mm.; *o*-dimethylaminophenol, 90–91° at 21 mm.; *p*-methylaminophenol, 172–173° at 22 mm.

These bases were then converted into their hydrochlorides by dissolving in dry ether and passing in dry hydrogen chloride. The precipitated hydrochlorides were washed with dry ether and dried in a vacuum.

The *p*-aminophenol hydrochloride of commercial grade was boiled in aqueous solution with animal charcoal, filtered and then crystallized by the addition of alcohol to the point where the total mixture was about 50%.

m-Aminophenol hydrochloride was made by the reduction of 50 g. of *m*-nitrophenol in butyl alcohol solution using 0.2 g. of platinum oxide and hydrogen at 3 atmospheres' pressure. The platinum black was filtered from the resulting solution and the hydrochloride precipitated by passing in dry hydrogen chloride. Upon partial evaporation of the solution in a vacuum and cooling it in ice, the hydrochloride separated.

The free base from commercial *o*-aminophenol hydrochloride was dissolved in an excess of dil. hydrochloric acid, the solution boiled with animal charcoal and then cooled in ice, whereupon the hydrochloride crystallized.

Reduction Procedure.—The procedure was similar to that described in previous papers in this series. The platinum oxide was added directly to the solution of hydrochloride in water, reduced in the usual way to platinum black and the reduction carried out at about 3 atmospheres'

[6] Wichers, THIS JOURNAL, **43**, 1268 (1921).

pressure. When complete, the reaction mixtures were worked up as follows. The platinum was filtered and the filtrate, which was usually turbid due to the formation of small amounts of cyclohexane, was made alkaline with solid sodium hydroxide until sodium chloride began to separate. The oil which was formed was then extracted several times with ether. The ether solution was dried over sodium sulfate, evaporated and the reaction products were distilled under diminished pressure.

Reduction of *p*-Dimethylaminophenol Hydrochloride.—From 40 g. of *p*-dimethylaminophenol hydrochloride in 200 cc. of water and 1.5 g. of U.S.P. sodium nitrate catalyst, 12 g. of low-boiling material distilling at 55–56° at 18 mm. or 161° at 740 mm. was proved by test to be cyclohexyl dimethylamine.

The second fraction, which amounted to about 10 g., distilled at 99–100° at 7 mm., 126° at 19 mm. or 228–229° at 740 mm.; d_{25}^{25}, 0.9830; n_D^{20}, 1.4859. At first it was considered that this was a single substance. The hydrochloride could be readily precipitated from dry ether in the form of white hygroscopic crystals which analyzed correctly according to the formula but did not melt sharply. The product, however, was later shown to be a mixture by the fact that two benzoate and two *p*-nitrobenzoate hydrochlorides could be obtained from it.

***p*-Dimethylaminocyclohexyl Benzoate Hydrochloride, α and β Forms,** $C_6H_5CO_2C_6H_{10}N(CH_3)_2.HCl$ (*p*).—Although several methods for preparing the benzoyl derivative were attempted, the only very satisfactory one found was to heat a mixture of one part of *p*-dimethylaminocyclohexanol hydrochloride with two parts of freshly distilled benzoyl chloride at 150° for three to four hours. After the mixture had cooled, dry ether was added and the ester hydrochloride precipitated. The solid product was recrystallized from boiling acetone to which just enough absolute alcohol was added to dissolve the material. After the first fraction which separated upon cooling had been filtered off, the filtrate was evaporated to one-half the original volume and a second fraction obtained. These two fractions on recrystallization from acetone and absolute alcohol as described above gave a product melting constantly at 243–244°, the α form.

Anal. Subs., 0.3593: 15.31 cc. of 0.1160 *N* $AgNO_3$. Calcd. for $C_{15}H_{21}O_2N.HCl$: Cl, 12.54. Found: 12.57.

The filtrate from the first two fractions was then evaporated until most of the alcohol had been driven off. Acetone was added at the boiling temperature and as the mixture cooled a third fraction was obtained. The mother liquors yielded a fourth fraction. These two fractions after mixing were recrystallized twice from a mixture of ethyl acetate and absolute alcohol and then melted constantly at 212.5–213.5°, the β form.

Anal. Subs., 0.4415: 15.45 cc. of 0.0995 *N* $AgNO_3$. Calcd. for $C_{15}H_{21}O_2N.HCl$: Cl, 12.54. Found: 12.35.

***p*-Dimethylaminocyclohexyl *p*-Nitrobenzoate Hydrochlorides, α and β Forms,** $(p)NO_2C_6H_4CO_2C_6H_{10}N(CH_3)_2HCl(p)$.—The *p*-dimethylaminocyclohexanol was condensed with 1 molecular equivalent of *p*-nitrobenzoyl chloride in hot chloroform. The chloroform was then evaporated and alcohol added. The first solid fraction after several crystallizations from butyl alcohol melted constantly at 250–252°, the α form.

Anal. Subs., 0.5026: 13.24 cc. of 0.1160 *N* $AgNO_3$. Calcd. for $C_{15}H_{20}O_4N_2HCl$: Cl, 10.79. Found: 10.83.

The filtrate from this material upon concentration gave a substance which upon recrystallization from butyl alcohol and then absolute alcohol melted at 233–234°, the β form.

Anal. Subs., 0.5001: 13.00 cc. of 0.1160 *N* $AgNO_3$. Calcd. for $C_{15}H_{20}H_4N_2HCl$: Cl, 10.79. Found: 10.69.

Reduction of *m*-Diethylaminophenol Hydrochloride.—From 50 g. of diethylaminophenol hydrochloride in 200 cc. and 1.5 g. of U. S. P. sodium-nitrate platinum oxide, 10 g. of a fraction boiling at 85–86° (20 mm.) was obtained. This was recognized as cyclohexyl-diethylamine[4] and boiled at 192–193° (740 mm.).

A second fraction of 25 g. distilled at 132–133° at 19–20 mm., or 245° at 740 mm.; d_{25}^{25}, 0.9503; n_D^{22}, 1.4850. It is not absolutely certain that this is a completely pure product. Nevertheless, only one benzoate and only one *p*-nitrobenzoate could be obtained. The hydrochloride was precipitated from dry ether as a pasty mass.

***m*-Diethylaminocyclohexyl Benzoate Hydrochloride,** $C_6H_5CO_2C_6H_{10}N(C_2H_5)_2HCl$ (*m*).—The same procedure was followed as in the benzoylation of the *para* compound. Precipitation with dry ether gave a product which after two crystallizations from ethyl acetate and absolute alcohol melted constantly at 148–150°. Further fractionation did not give rise to a second isomer.

Anal. Subs., 0.5308: 14.91 cc. of 0.1160 *N* $AgNO_3$. Calcd. for $C_{17}H_{25}O_2N.HCl$: Cl, 11.38. Found: 11.55.

***m*-Diethylaminocyclohexyl *p*-Nitrobenzoate Hydrochloride,** (*p*)$NO_2C_6H_4CO_2C_6H_{10}N(C_2H_5)_2.HCl$ (*m*).—One part of the alcohol and two parts of *p*-nitrobenzoyl chloride were heated together at 150° for one hour. The product was precipitated from dry ether and recrystallized from acetone. It melted at 161–163°. No second isomer could be isolated.

Anal. Subs., 0.5040: 14.27 cc. of 0.0995 *N* $AgNO_3$. Calcd. for $C_{17}H_{24}O_4N_2HCl$: Cl, 9.94. Found: 9.99.

Reduction of *m*-Dimethylaminophenol Hydrochloride.—From 50 g. of dimethylaminophenol hydrochloride in 200 cc. of water with 1.5 g. of U. S. P. sodium-nitrate platinum oxide was obtained 9 g. of a fraction boiling at 56° at 20 mm., or 161° at 740 mm. This proved to be cyclohexyl-dimethylamine.

The second fraction, which distilled at 126–127° at 22 mm., weighed about 25 g. and boiled at 231° at 740 mm.; d_{25}^{25}, 0.9766; n_D^{22}, 1.4846. The hydrochloride was obtained as a pasty mass by adding dry hydrogen chloride to a dry ether solution.

This base must be practically a pure substance since only one benzoate and only one *p*-nitrobenzoate hydrochloride could be obtained.

***m*-Dimethylaminocyclohexyl Benzoate Hydrochloride,** $C_6H_5CO_2C_6H_{10}N(CH_3)_2HCl$ (*m*).—This substance was made in chloroform solution. After evaporation of the solvent, the product was dissolved in ethyl acetate and recrystallized to a constant melting point of 229–230°.

Anal. Subs., 0.5049: 15.54 cc. of 0.1160 *N* $AgNO_3$. Calcd. for $C_{15}H_{21}O_2N.HCl$: Cl, 12.54. Found: 12.66.

***m*-Dimethylaminocyclohexyl *p*-Nitrobenzoate Hydrochloride,** (*p*)$NO_2C_6H_4CO_2C_6H_{10}N(CH_3)_2.HCl$ (*m*).—The condensation was carried out in hot chloroform. After evaporation of the latter butyl alcohol was added and the product recrystallized from this solvent to a constant melting point of 224–225°.

Anal. Subs., 0.5009: 13.15 cc. of 0.1160 *N* $AgNO_3$. Calcd. for $C_{15}H_{20}O_4N_2HCl$ Cl, 10.79. Found: 10.80.

Reduction of *p*-Methylaminophenol Hydrochloride.—From 20 g. of *p*-methyl-aminophenol hydrochloride in 100 cc. of water and 0.75 g. of U. S. P. sodium-nitrate platinum oxide, 5 g. of methylaminocyclohexane[4] was obtained boiling at 147–148° (740 mm).

A second fraction boiling at 134–135° at 23–24 mm., or 229–230° at 740 mm. crystallized upon cooling and melted at 78°. The hydrochloride, prepared by precipi-

tation from dry ether, melted at 121–135° after crystallization from ethyl acetate and absolute alcohol, suggesting the presence of isomers. The hydrochloride was analyzed and gave the correct analysis.

Anal. Subs., 0.3155: 19.08 cc. of 0.0995 *N* $AgNO_3$. Calcd. for $C_7H_{15}ON.HCl$: Cl, 21.43. Found: 21.35.

No attempt was made to prepare the benzoates or *p*-nitrobenzoates in order to separate the isomers.

Reduction of *m*-Aminophenol Hydrochloride.—From 20 g. of *m*-aminophenol hydrochloride in 100 cc. of water and 0.75 g. of U. S. P. sodium-nitrate platinum oxide there was obtained 1 g. of cyclohexylamine[4] which was recognized by the melting point of its hydrochloride, 204–205°.

A second fraction weighed about 4 g. and boiled at 118–120° (17 mm.). The hydrochloride of this base after crystallization from absolute alcohol melted at 339–342°. Skita[4] reports the melting point of dicyclohexylamine hydrochloride as 344°.

Anal. Subs., 0.1992: 9.22 cc. of 0.0995 *N* $AgNO_3$. Calcd. for $C_{12}H_{23}N.HCl$: Cl, 16.30. Found: 16.34.

A third fraction distilled at 170° (12 mm.), solidified upon cooling and melted at 121–122°. The hydrochloride, made by precipitation with dry hydrogen chloride from alcohol solution, after purification from absolute alcohol melted at 289–291° and was proved by analysis to be the hydrochloride of *m*-cyclohexylamino-cyclohexanol, HOC_6H_{10}-$NHC_6H_{11}.HCl$ (*m*).

Anal. Subs., 0.2553: 10.93 cc. of 0.0995 *N* $AgNO_3$. Calcd. for $C_{12}H_{23}ON.HCl$: Cl, 15.19. Found: 15.11.

Summary

1. Various aminophenols have been reduced to cyclic amino-alcohols by means of platinum-oxide platinum black and hydrogen under 2 to 3 atmospheres' pressure. There was always formed simultaneously the corresponding cyclohexylamine.

2. In the case of *p*-dimethylaminophenol hydrochloride a mixture of *cis* and *trans* isomers was obtained which could be separated in the form of the benzoate or *p*-nitrobenzoate hydrochlorides. The *meta* compounds, however, apparently yielded only a single isomer upon reduction.

3. Of the unsubstituted aminophenols only the *m*-aminophenol reduced readily. This yielded no *m*-aminocyclohexanol but cyclohexylamine, dicyclohexylamine and *m*-cyclohexylamino-cyclohexanol.

4. The activity of the catalyst has been shown to be considerably affected by the presence of traces of impurities.

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