(1) the preparation of the enzyme in the form of a highly purified product of maximum activity and uniform properties and the analysis of these purified preparations with reference to their qualitative reactions, quantitative elementary composition, and the kinds and amounts of amino acid radicals which they contain as determined by the Van Slyke method; (2) quantitative study of the comparative effects of different antiseptics, those characterized by their chemical action upon proteins being found very much more destructive than those of the lipoid-dissolving type; (3) investigation of the inactivating action of warm water upon the enzyme and the effects of amino acids in retarding this inactivation. The data of these three lines of evidence are entirely consistent and all point to the protein nature of the enzyme.

That malt amylase is also of a protein nature has been rendered in the highest degree probable by similar studies and by the further observation that it resembles typical proteins in showing an iso-electric point in electrophoresis experiments and that the iso-electric point thus established bears a definite relation to the activity, as it coincides with the hydrogen-ion concentration at which optimum activity occurs.[8] Studies of the iso-electric point of pancreatic amylase, while much more difficult because of its greater sensitiveness to deterioration, are being undertaken.

We are greatly indebted to the Carnegie Institution of Washington for grants in aid of this investigation.

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[Contribution from the Bureau of Chemistry, United States Department of Agriculture]

TOLUIDINE DERIVATIVES. I. QUANTITATIVE PREPARATION OF 5-IODO-2-AMINOTOLUENE AND SOME OF ITS DERIVATIVES

By Raymond M. Hann and Julius F. T. Berliner

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Iodo-*o*-toluidine (5-iodo-2-aminotoluene) has been prepared by Artmann[1] and by Wheeler and Liddle.[2] After several unsuccessful attempts to obtain satisfactory yields by this method,[3] we modified their general procedure as follows.

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[8] Sherman, Thomas and Caldwell, This Journal, **46**, 1711 (1924).

[1] Artmann, *Monatsh.*, **26**, 1097 (1905).

[2] Wheeler and Liddle, *Am. Chem. J.*, **42**, 501 (1909). See also Fichter and Philipp, *J. prakt. Chem.*, **74**, 312 (1906); Willgerodt and Heusner, *Ber.*, **40**, 4077 (1907). The complete series of possible iodine nuclear derivatives of toluene are described by Wheeler, *Am. Chem. J.*, **44**, 493 (1910).

[3] Dains, Malleis, and Meyers [This Journal, **35**, 970 (1913)] report "good results" from preparing 5-iodo-toluidine by Wheeler and Liddle's method. The yield is not stated, however.

The hydrochloride of *o*-toluidine is readily attacked by iodine, and the liberated hydriodic acid is at once taken up by the calcium carbonate without intermediate formation of the base hydriodide. By this procedure the heating and tar-like formation, which occur when iodine is added directly to *o*-toluidine, are avoided. The reaction product was extracted with ether, thus eliminating the lengthy steam distillation which we found to result in the formation of a tar-like substance. The yield of the crude product was approximately 99%.

The halogenation of an aromatic amine may be a more complex reaction than simple substitution. It is not improbable that the formation of an intermediate compound, in which nitrogen is directly attached to the halogen, enters into the mechanism of halogen substitution. Such a compound was obtained by Wheeler and Morse[4] in the course of their experiments on the chlorination of the acetyl derivative of 2-amino-*p*-xylene. Chattaway[5] has shown that diamines readily substitute halogen to form tetrahalogen diamines of the general class $Br_2N-CH_2-CH_2-NBr_2$. Johnson[6] and his co-workers showed that bromination of amines in which tribromination takes place proceeds in three stages, the first two being simultaneous. Finally, dihalogenated Schiff's bases when hydrolyzed yield the aldehyde from which they were prepared and the *para*-halogenated hydro-halide of the original amine.

Experimental Part

5-Iodo-2-aminotoluene.—Forty g. of dry *o*-toluidine hydrochloride and 71 g. of dry powdered iodine were triturated together; 35 g. of precipitated calcium carbonate was then ground into the intimate mixture. The resulting product was transferred to an Erlenmeyer flask, and 200 cc. of distilled water was added while vigorously shaking the flask. The flask was then allowed to stand for about three-quarters of an hour, during occasional agitation, after which it was heated gradually to 60° or 70° for five minutes and cooled. The contents of the flask were transferred to a large separatory funnel. The solution was extracted with 500 cc. of ether in three portions and the extract was dried with calcium chloride. On removing the excess of solvent, the iodinated base separated in dark, blade-like crystals; yield, 63.8 to 64.3 g., or 98.2 to 98.9%. The crude product may be used directly or it may be recrystallized from petroleum ether or 50% alcohol, preferably the latter.

By this method 5-iodo-2-aminotoluene is obtained as a nearly white

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[4] Wheeler and Morse, THIS JOURNAL, **46**, 2572 (1924).

[5] Chattaway, *J. Chem. Soc.*, **87**, 381 (1905).

[6] Johnson, Hill and Francis. Presented in a paper on "A Study of Directing Influence of Substituents in the Benzene Ring by Means of Rate of Bromination" at the meeting of the American Chemical Society, Washington, D. C., April 21–26, 1924.

TABLE I

DERIVATIVES OF 5-IODO-ORTHO-TOLUIDINE

Reagent	Formula of compound	Solvent	Solubility	Crystalline form	Color	M. p. (Corr.) ° C.	Analysis (Kjeldahl-Gunning-Arnold) Subs. G.	0.1 *N* acid consumed Cc.	N found %	N calcd. %
HCl	R.HCl	Alcohol	Alcohol	Needles	Colorless	214	0.1223	4.6	5.27	5.20
HBr	R.HBr	Alcohol	Alcohol	Leaflets	Colorless	196	.1230	3.8	4.33	4.46
HI	R.HI	Ether	Water, alcohol	Plates	Colorless	190	.1205	3.8	4.42	4.47
H_2F_2	$R.(HF)_4$[a]	Ether	Water, alcohol	Needles	Colorless	105	.2056	5.3	3.61	3.88
$HClO_4$	$R.HClO_4$	Alcohol	Alcohol	Plates	Colorless	209	.1272	3.9	4.29	4.20
$C_6H_2(NO_2)_3OH$	$R.C_6H_2(NO_2)_3OH$	Alcohol	Alcohol	Needles	Yellow	188.5	.2005	17.25	12.05	12.13
Picrolonic acid	5-Iodo-*o*-toluidine Picrolonate	Alcohol	Alcohol	Needles	Yellow	189.5	.2000	20.0	14.01	14.08
$(COOH)_2$	$2R.(COOH)_2$	Alcohol	Alcohol	Needles	White	158	.1890	6.7	4.96	5.04
$HgCl_2$	$2R.HgCl_2$	Alcohol	Alcohol	Needles	Gray	134.5	.1275	3.3	3.63	3.79

[a] The hydrofluoric acid compounds of amines will be treated in a forthcoming paper.

TABLE II

5-IODO-ORTHO-TOLYL DERIVATIVES

Reagent	Compound formula	Solvent	Solubility	Crystalline form	Color	M. p. (Corr.) ° C.	Analysis (Kjeldahl-Gunning-Arnold) Subs. G.	0.1 *N* acid consumed Cc.	N found %	N calcd. %
KNCO	$RNHCONH_2$	Acetic acid	Alcohol	Needles	Colorless	273	0.1086	7.8	10.06	10.14
$RNHCONH_2+HCl$	$RNHCONH_2.HCl$	Alcohol	Alcohol	Needles	Colorless	Sublimed	.1096	7.3	9.33	8.96
C_6H_5NCO	$RNHCONHHC_6H_5$	Alcohol	Alcohol	Needles	Colorless	232	.1015	5.8	8.00	7.96
α-$C_{10}H_7NCO$	α-$C_{10}H_7NHCONHR$	Alcohol	Alcohol	Powder	Gray	214	.1109	5.5	6.95	6.97
$CHCl_3 + KOH$	R.NC	Alcohol	Ether Me alcohol Alcohol	Needles	Yellow	83–84	.1455	5.9	5.61	5.76

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.

WASHINGTON, D. C.

[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]

BY HERMANN HECKEL[2] WITH ROGER ADAMS

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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-

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[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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