rated acid was converted through its acid chloride to the acylmalonic ester and then hydrolyzed and decarboxylated as previously described, 0.27 g. (62%) of crude crystalline ketone, m. p. 153–158°, was obtained in three crops from 95% ethanol. Recrystallization of this material gave 0.20 g. (46%) of solid, m. p. 158–160°. The analytical sample was obtained from ethanol in the form of thick hexagonal plates, m. p. 159–160°.

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.0; H, 8.2. Found: C, 80.9; H, 7.9.

When 0.40 g. of the acetoxy saturated acid was converted to the acid chloride, treated with dimethylcadmium following the procedure described for the stilbene analog, and the oily acetoxy ketone hydrolyzed, 0.33 g. of crude solid hydroxy ketone was obtained, m. p. 147–153°. Two recrystallizations from 95% ethanol gave 0.22 g. (63%) of the ketone, m. p. 158–160°.

The methyl ether, prepared from the above saturated phenolic ketone with dimethyl sulfate, crystallized from acetone-petroleum ether as colorless platelets, m. p. 135.5–137°.

Anal. Calcd. for $C_{21}H_{26}O_2$: C, 81.3; H, 8.4. Found: C, 81.0; H, 8.1.

α,α′-Diethyl-4′-acetoxy-4-acetoxyacetylstilbene (IX).—The acid chloride from 1.00 g. of the acetoxystilbene acid dissolved in 10 cc. of dry benzene was added dropwise to a cold (0–5°) ethereal solution of diazomethane (prepared from 4.4 g. of nitrosomethylurea, dried over potassium hydroxide and distilled). After standing at room temperature for nineteen hours, the excess diazomethane and ether were removed leaving the crude solid diazoketone (1.02 g.). Recrystallization from benzene-petroleum ether gave 0.88 g. (82%) of the pale yellow compound, m. p. 152–154° (dec.). To 2 cc. of boiling acetic acid was added 200 mg. of the recrystallized diazoketone. Nitrogen was rapidly evolved and boiling was continued five minutes after the addition was complete. The mixture was chilled, taken up in ether and washed with water. Evaporation of the dried ether extract left a semisolid residue which was recrystallized from ethanol to give in two crops 189 mg. of solid, m. p. 123–137°. Further recrystallization from acetone-petroleum ether resulted in 144 mg. of the stilbene acetoxyacetyl derivative, m. p. 135–138°, corresponding to a 66% yield from the diazoketone or 54% from the acetoxy acid. Further recrystallization gave the pure compound as thick, colorless prisms which showed two melting points, 133.2–134° and 138–140°.

Anal. Calcd. for $C_{24}H_{26}O_5$: C, 73.1; H, 6.6. Found: C, 73.0; H, 6.6.

The over-all yield of the acetoxy ketone was higher (63%) when the intermediate diazoketone was not recrystallized but used directly. An attempt to obtain more crystalline material from the oily residue by chromatographic adsorption on alumina gave only a negligible amount of impure solid, m. p. 100–125°.

3-(*p*-Acetoxyacetylphenyl)-4-(*p*-acetoxyphenyl)-hexane (XI).—One hundred milligrams of the saturated acetoxy acid was converted through the diazoketone to the acetoxyacetyl derivative by the above procedure; a first crop of 36 mg., m. p. 150–152°, was obtained from acetone-petroleum ether and another 41 mg., m. p. 135–147°, in three additional crops. Recrystallization of the latter material brought the yield of saturated acetoxy ketone to 70 mg. (60%), m. p. 149–152°. Several more recrystallizations gave the pure compound as long, colorless blades, m. p. 152–153.5°.

Anal. Calcd. for $C_{24}H_{28}O_5$: C, 72.7; H, 7.1. Found: C, 72.6; H, 7.0.

Summary

Some analogs of progesterone and desoxycorticosterone have been prepared in the stilbestrol and hexestrol series.

These crystalline compounds, as well as mixtures of isomers corresponding to them, were found to be weak estrogens but failed to show progestational or adrenal cortical activity.

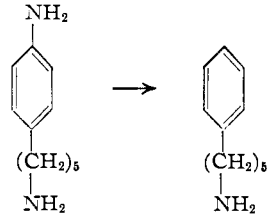
MADISON 6, WIS. RECEIVED FEBRUARY 8, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Selective Replacement of the Aromatic Primary Amino Group by Hydrogen in Aromatic–Aliphatic Diamines[1]

BY NATHAN KORNBLUM AND DON C. IFFLAND[2]

It has recently been found in this Laboratory that aliphatic primary amines do not react with nitrous acid at a *p*H below *ca.* 3.[3] Thus, methylamine, ethylamine, *n*-propylamine, *n*-amylamine, benzylamine and cyclohexylamine are not attacked by nitrous acid below this *p*H. In sharp contrast, aromatic primary amines are routinely diazotized at a *p*H below 1, *i.e.*, in relatively strongly acidic solutions.[4] This difference, plus the fact that hypophosphorous acid smoothly replaces a diazonium group by hydrogen,[5] now makes it possible to effect transformations such as



That is, an aromatic primary amino group is replaced by hydrogen without disturbing the aliphatic amino group. The selective deamination reaction is a general one as is demonstrated by its successful application to a total of thirteen aromatic–aliphatic diamines in which the side chains are ortho, meta and para to the aromatic amino group.

The procedure is very simple; hypophosphorous acid being a relatively strong acid[6] is used not only as the reducing agent but also as the source

(1) From the doctoral dissertation of Don C. Iffland, Purdue University, June, 1947.

(2) Present address: University of West Virginia, Morgantown, West Va.

(3) Iffland, Ph.D. thesis, Purdue University, June, 1947.

(4) "Organic Syntheses," Coll. Volume I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 542; Saunders, "The Aromatic Diazo Compounds," Arnold and Co., London, 1936, p. 4.

(5) Kornblum, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. II, pp. 277–282.

(6) $K = 6 \times 10^{-2}$; Kolthoff, *Rec. trav. chim.*, **46**, 350 (1927)

TABLE I

SUMMARY OF SELECTIVE DEAMINATIONS

	Diamine	Monoamine	Yield, %	B. p., °C.	Mm.	$n^{20}D$	N Analyses, % Calcd.	N Analyses, % Found	Benzoyl deriv. of monoamine M. p., °C.	N Analyses, % Calcd.	N Analyses, % Found
I	*m*-H_2N-C_6H_4-CH_2NH_2	Benzylamine	87	183–184		1.5376[a]					
II	*p*-H_2N-C_6H_4-CH_2NH_2	Benzylamine	84	181–183		1.5372[a]					
III	*o*-H_2N-C_6H_4-$CH_2CH_2NH_2$	β-Phenylethylamine	52	83–84	13	1.5340			114–115[d]		
IV	*m*-H_2N-C_6H_4-$CH_2CH_2NH_2$	β-Phenylethylamine	70	82–84	14	1.5342			115–116[d]		
V	*p*-H_2N-C_6H_4-$CH_2CH_2NH_2$	β-Phenylethylamine	71	85–86	13	1.5340			115.5–116[d]		
VI	*p*-H_2N-C_6H_4-$CH_2CH(NH_2)CH_3$	1-Phenyl-2-amino-propane[e]	78	91	15[f]	1.5185					
VII	*p*-H_2N-C_6H_4-$CH_2C(NH_2)(CH_3)_2$	1-Phenyl-2-amino-2-methylpropane	79	94	15	1.5132	9.38	9.42 9.48	112.5–113	5.53	5.43
VIII	*p*-H_2N-C_6H_4-$CH_2CH(NH_2)C_2H_5$	1-Phenyl-2-amino-butane	77	106	15	1.5142	9.38	9.18	122–122.5	5.53	5.44 5.42
IX	*p*-H_2N-C_6H_4-$CH_2C(NH_2)(CH_3)C_2H_5$	1-Phenyl-2-amino-2-methylbutane	70	111	14	1.5147	8.58	8.56	113.5–114	5.24	5.22
X	*p*-H_2N-C_6H_4-CH_2-$CH(NH_2)CH_2CH_2CH_3$	1-Phenyl-2-amino-pentane	67	118	15	1.5084	8.58	8.47	123–123.5	5.24	5.16 5.18
XI	*p*-H_2N-C_6H_4-$CH_2C(NH_2)CH_2CH_2CH_2CH_2$	1-Benzyl-1-amino-cyclopentane	73	119	6	1.5374	7.81	7.91	123.5–124	5.01	4.99
XII	*p*-H_2N-C_6H_4-CH_2-$C(NH_2)CH_2CH_2CH_2CH_2CH_2$	1-Benzyl-1-amino-cyclohexane	74	140	10	1.5398	7.40	7.56	101.5–102	4.78	4.80
XIII	*p*-H_2N-C_6H_4-$CH_2CH_2CH_2CH_2CH_2NH_2$	1-Phenyl-5-amino-pentane	60	[b]		1.5130[c]	8.58	8.51 8.38			

[a] n_D taken at 26°; the picrates prepared from these products melt 194–195°. The accepted m. p. is 196° [McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945, p. 206]. [b] The amount of monoamine available was too small to obtain a reliable b. p. It was distilled at 15 mm. and a bath temperature of 140–160°; von Braun [*Ber.*, **43**, 2849 (1911)] reported b. p. 135° (15 mm.). von Braun also reported the m. p. of the picrate as 152–153°; the picrate of the present sample of 1-phenyl-5-aminopentane, crystallized from benzene, melts at 156–157°. [c] n_D taken at 25°. [d] Michaelis and Linow [*Ber.*, **26**, 2167 (1893)] reported m. p. 116°. [e] Picrate melts at 144–145° (cor.); lit.value 143°, Hey [*J. Chem. Soc.*, 18 (1930)]. [f] At 750 mm. b. p. is 197–198°; Hey [*J. Chem. Soc.*, 18 (1930)] reports b. p. 205°; Edeleano [*Ber.*, **20**, 618 (1887)] found b. p. 203°.

of required acidity. The diamine is dissolved in hypophosphorus acid, sodium nitrite is added at 0 to 5°, and the mixture is then allowed to come to room temperature; after three to five hours the reaction is complete. The yields of pure products are excellent; *cf.* Table I.

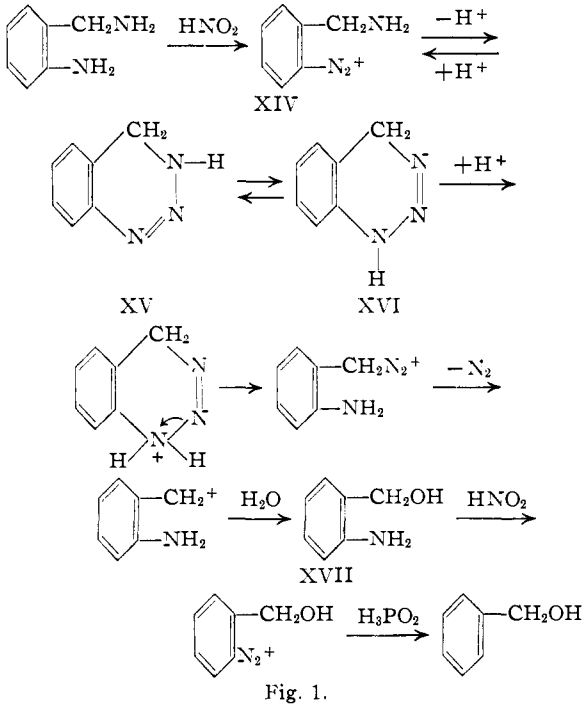


Fig. 1.

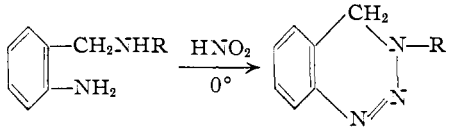
The selective replacement of an aromatic primary amino group by hydrogen may also be accomplished by first diazotizing in the ordinary way with sodium nitrite and hydrochloric acid and then adding hypophosphorous acid. When diamines VIII and XII were selectively deaminated in this way the yields were 67 and 83%, respectively, *i.e.*, essentially the same as for the first method. This procedure, unlike the first one, can obviously be extended to the selective replacement of an aromatic primary amino group by a variety of other atoms or groups since, instead of reducing the diazonium group with hypophosphorous acid, other reactions of the diazonium compounds may be invoked.

The only diamine which fails to undergo the selective deamination reaction is *o*-aminobenzylamine. Instead of benzylamine, benzyl alcohol is obtained; when hydrochloric acid is present the product is benzyl chloride. It is noteworthy, however, that benzylamine is not an intermediate in these transformations as is shown by its recovery in 89–92% yield after treatment with sodium nitrite in the presence of hypophosphorous acid or hydrochloric acid under the conditions of the selective deamination reaction. This lack of reactivity is, of course, an illustration of the

*p*H requirement mentioned in the first sentence of this paper.

The remarkable conversion of *o*-aminobenzylamine to benzyl alcohol (or benzyl chloride) is readily explained by the sequence shown.

The assumption that XV is an intermediate is justified by the fact that numerous examples of the reaction XVIII → XIX are known.[7] Busch's observation[7] that *o*-aminobenzylamine gives none of the corresponding heterocycle (XV) at first sight may seem to controvert this idea. Actually, as will be seen below, Busch's inability to isolate XV is fully consistent with the proposed mechanism for the conversion of *o*-aminobenzylamine to benzyl alcohol.

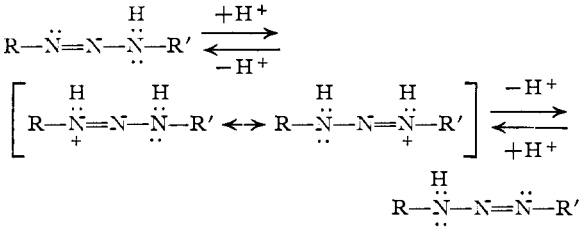


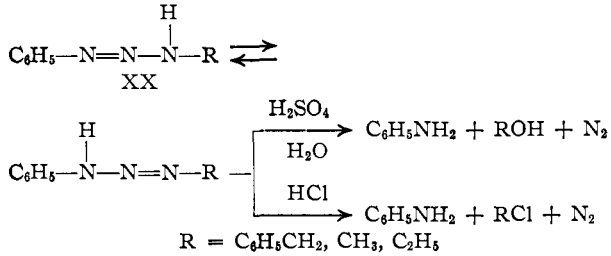
XVIII XIX

R = CH_3, C_2H_5, C_6H_5, $C_6H_5CH_2$, etc.

Cyclic compound XV is a diazoamino compound and as such would at once come to tautomeric equilibrium with diazoamino compound XVI.[8] The acid-catalyzed transformation of XVI to XVII (or in the presence of hydrochloric acid to *o*-aminobenzyl chloride) involves nothing more than the well known cleavage of diazoamino compounds by acids. The indicated mode of cleavage employing XVI rather than its tautomer XV is amply justified by Dimroth's studies on the acid-catalyzed decomposition of mixed aromatic-aliphatic diazoamino compounds such as XX.[9] These compounds are extraordinarily sensitive to acids; even at 0° they are rapidly and quantitatively split by dilute sulfuric or hydrochloric acids to the aromatic amine and the decomposition products of the aliphatic diazonium salt[10]

The final stage of the proposed sequence calls for the formation of benzyl alcohol from *o*-aminobenzyl alcohol (XVII), a reaction which takes





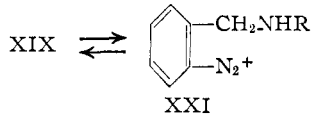
XX

R = $C_6H_5CH_2$, CH_3, C_2H_5

place readily when *o*-aminobenzyl alcohol is treated with sodium nitrite and hypophosphorous acid.[11]

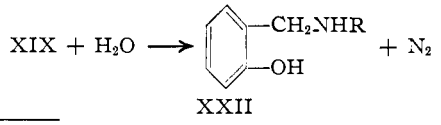
It is an important feature of the proposed mechanism that a path is employed which is not available to the other diamines. This serves to explain the unique inability of *o*-aminobenzylamine to undergo the selective deamination reaction.[12]

The proposed mechanism also offers a simple explanation of Busch's observation[7] that the reaction of *o*-aminobenzylamine with nitrous acid did not follow the usual pattern XVIII → XIX. Instead, copious amounts of nitrogen were formed and an organic product which could not be purified was obtained. From the point of view of the foregoing discussion this behavior is perfectly reasonable since only *o*-aminobenzylamine gives a heterocycle (XV) which can tautomerize to an isomeric diazoamino compound of the type represented by XVI. Diazoamino compound XVI (or a homolog) upon being split by acids yields an aliphatic diazonium salt and this rapidly loses nitrogen in the manner indicated in Fig. 1. In contrast, heterocycles such as XIX are relatively stable in cold acid solutions. Here, since tautomerism is not possible, ring opening can only occur in the sense XIX → XXI



XXI

and compound XXI, being an aromatic diazonium salt, will not break down rapidly at 0°. As one would anticipate, aqueous solutions of the salts of XIX decompose on gentle warming giving nitrogen and the substituted *o*-aminomethylphenol XXII



XXII

(7) Busch, *J. prakt. Chem.*, [2] **51**, 113 (1895); [2] **51**, 257 (1895); [2] **52**, 373 (1895).

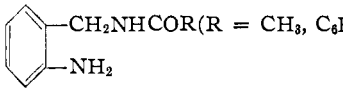
(8) J. W. Baker, "Tautomerism," D. Van Nostrand Co., Inc., New York, N. Y., 1934, pp. 143-147; T. W. J. Taylor and W. Baker, "Sidgwick's Organic Chemistry of Nitrogen," new ed., Clarendon Press, Oxford, 1937, p. 460. The facile interconversion of the tautomeric forms of diazoamino compounds in acid solution is easily understandable:

(9) Dimroth, *Ber.*, **38**, 670 (1905).

(10) Acetic acid, and even carbonic acid, also catalyze this cleavage of mixed aromatic-aliphatic diazoamino compounds although not as effectively as the mineral acids; *cf.* ref. 9.

(11) Our thanks are due to Mr. G. D. Cooper of this Department for carrying out this experiment.

(12) An alternative explanation, which is at present less easily evaluated, is based on the argument that in XIV the basicity of the aliphatic amino group is reduced sufficiently to permit it to react with nitrous acid under the prevailing conditions. It seems likely that *o*-aminobenzylamine can be selectively deaminated to benzylamine if acylated derivatives of the type



are employed. This possibility is being investigated.

in concentrated hydrochloric acid the corresponding *o*-chlorobenzylamine is obtained.[7]

Diamines VI–XII were kindly supplied by Professor H. B. Hass; their preparation is described in the accompanying paper.[13] The synthesis of the remaining diamines is detailed in the experimental portion of this paper. Perhaps the most interesting feature of the synthetic work was the repeated demonstration of the utility of the Schmidt reaction.[14]

Acknowledgment.—We wish to express our thanks to the Purdue Research Foundation for an X-R Fellowship and other financial assistance.

Experimental[15]

Selective Deamination Procedures

Selective Deamination Procedures. Procedure I.—Only the selective deamination of *p*-aminobenzylamine is described since it is typical. The yields reported in Table I were obtained by this procedure.

To a 200-ml. flask containing 3.65 g. (0.03 mole) of *p*-aminobenzylamine, 60 g. (0.45 mole)[16] of 50% aqueous hypophosphorous acid was added. The resulting solution was diluted with 50 ml. of water and then cooled to 5°. While stirring, a solution of 2.3 g. (0.033 mole) of sodium nitrite in 10 ml. of water was run in dropwise (ten to fifteen minutes). The reaction mixture was then stirred gently for a half-hour at 5°[17] and finally allowed to come to room temperature and stand for about four hours. After rendering strongly alkaline with sodium hydroxide, the product was continuously extracted with ether. The extract was dried over potassium hydroxide pellets and then distilled. There was obtained 2.67 g. (84% yield) of benzylamine; b.p. 181–183°; $n^{26}D$ 1.5372; picrate, m. p. 194–195°.

Procedure II.—Five and one-tenth grams (0.025 mole) of 1-(*p*-aminobenzyl)-1-aminocyclohexane[18] was dissolved in a mixture of 9.0 ml. (0.1 mole) of 37% hydrochloric acid and 35 ml. of water. The solution was cooled to 5° and, while stirring, 2.0 g. (0.030 mole) of sodium nitrite in 15 ml. of water was added. Stirring was continued for ten minutes after the nitrite had been run in and then 50 g. (0.375 mole) of 50% hypophosphorous acid (precooled to 0°) was added. After an additional fifteen minutes, stirring was discontinued and the reaction mixture allowed to stand for six hours at room temperature. The product was then isolated as in Procedure I. The yield of 1-benzyl-1-aminocyclohexane was 3.9 g. (83%); b. p. 135° (7 mm.); $n^{20}D$ 1.5398.

Preparation of *o*-Aminobenzylamine.—A solution of 14.8 g. (0.1 mole) of *o*-nitrobenzonitrile[18] in 60 ml. of acetic anhydride was shaken with hydrogen at three atmospheres in the presence of 0.1 g. of Adams catalyst. Hydrogen uptake was rapid until three-fifths the theoretical amount had been absorbed. Fresh catalyst was added and shaking was continued until the calculated amount of hydrogen had been absorbed (about thirty-six hours). The reduction mixture was filtered, made alkaline with a solution of 100 g. of sodium hydroxide in 250 ml. of water and refluxed twenty-four hours in a nitrogen atmosphere. Upon cooling, the product was continuously extracted with ether and the extract was dried over potassium hydroxide pellets. The solvent was removed and the residue vacuum distilled; 5.3 g. of a colorless liquid b. p. 85–90° (1 mm.) was obtained. On standing a short time it crystallized; m. p. 57–59°. After recrystallization from petroleum ether the diamine melted at 59–59.5°. *Anal.* Calcd. for $C_7H_{10}N_2$: N, 22.95. Found: N, 22.43, 22.70. Gabriel[19] reported m. p. 50°.

The diacetyl derivative melts at 137–138°; lit. value,[19] 136–137°. The dibenzoyl derivative melts 193–193.5°.

Anal. Calcd. for $C_{21}H_{18}O_2N_2$: C, 76.34; H, 5.49; Found: C, 76.09; H, 5.61.

Preparation of *m*-Aminobenzylamine. (a) *m*-Nitrobenzyl Alcohol.—*m*-Nitrobenzaldehyde was reduced to *m*-nitrobenzyl alcohol using aluminum isopropoxide and isopropyl alcohol; the procedure for the reduction of benzaldehyde described by Wilds[20] was carefully followed; yield 85%; b. p. 168–170° (6 mm.), lit. b. p.[21] 175–180° (3 mm.); $n^{28}D$ 1.5731.

(b) *m*-Nitrobenzyl bromide.—A solution of 76 g. (0.5 mole) of *m*-nitrobenzyl alcohol in 150 ml. of toluene was cooled in an ice–salt-bath and, with efficient stirring, 148 g. (0.55 mole) of phosphorus tribromide was added slowly enough to keep the temperature below 0°. The reaction mixture was then stirred a half-hour at 0° and five hours on a steam cone. Upon cooling, the toluene solution was poured over 400 g. of ice; the toluene layer was separated and washed successively with two 25-ml. portions of concentrated sulfuric acid, water, aqueous sodium bicarbonate and again with water. The toluene solution was concentrated to about 100 ml. and then 300 ml. of petroleum ether (b. p. 30–60°) was added. This solution was cooled in ice and the *m*-nitrobenzyl bromide which crystallized was filtered and washed with 100 ml. of cold petroleum ether; yield 91 g. (85%); m. p. 57–58°; lit. value,[22] m. p. 58–59°.

(c) N-(*m*-Nitrobenzyl)-phthalimide.—A mixture of 75 g. (0.35 mole) of *m*-nitrobenzyl bromide and 75 g. (0.42 mole) of potassium phthalimide was heated at 180–200° for five hours. The product was crushed, thoroughly washed with hot water and crystallized from glacial acetic acid. Seventy grams of N-(*m*-nitrobenzyl)-phthalimide was obtained; yield, 73%; m. p. 162–163°; lit. m. p. 155°.[23]

Anal. Calcd. for $C_{15}H_{10}N_2O_4$: N, 9.92. Found: N, 9.76.

(d) N-(*m*-Aminobenzyl)-phthalimide.—A suspension of 25 g. of N-(*m*-nitrobenzyl)-phthalimide and 0.2 g. platinum oxide in 150 ml. of glacial acetic acid was shaken with hydrogen at 3 atm. until the theoretical amount of hydrogen was absorbed. The reduction product was diluted with an equal volume of water, filtered and made alkaline with sodium hydroxide. The N-(*m*-aminobenzyl)-phthalimide, which precipitated, was isolated by filtration and crystallized from aqueous ethanol. A 63% yield of yellow needles was obtained; m. p. 127–128°; lit. value 118°.[24]

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: N, 11.11. Found: N, 11.10.

(e) *m*-Aminobenzylamine.—Hydrolysis of N-(*m*-aminobenzyl)-phthalimide was accomplished with hydrazine hydrate in the usual way[25]; b. p. 133–134° (4 mm.); $n^{20}D$ 1.6092; yield 60%.

Anal. Calcd. for $C_7H_{10}N_2$: N, 22.95; Found: N, 23.05, 22.87.

The dibenzoyl derivative of *m*-aminobenzylamine melts at 173–174°.

(13) Hass, Berry and Bender, THIS JOURNAL, **71**, in press (1949).

(14) H. Wolff, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1946, Vol. III. p. 327.

(15) Microanalyses by H. Galbraith and L. Roth of this Department.

(16) Fifteen moles of hypophosphorous acid was employed per mole of diamine. No study has been made showing that this is an optimum ratio; quite possibly equally good results will be obtained using much less hypophosphorous acid.

(17) This temperature does not seem to be very critical; in some runs it was close to 0° and in others up around 8° yet the yields remained substantially the same.

(18) Bogert and Hand, THIS JOURNAL, **20**, 1035 (1902).

(19) Gabriel, *Ber.*, **20**, 2229 (1887).

(20) Wilds, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. II, p. 201.

(21) Grimaux, *Compt. rend.*, **65**, 211 (1867).

(22) Norris, Watt and Thomas, THIS JOURNAL, **38**, 1077 (1916).

(23) Gabriel and Hendess, *Ber.*, **20**, 2869 (1887).

(24) Hafner, *Ber.*, **23**, 341 (1890).

(25) Ing and Manske, *J. Chem. Soc.*, 2348 (1926).

Anal. Calcd. for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.50; Found: C, 76.29; H, 5.63.

Preparation of *p*-Aminobenzylamine. (a) **N-(*p*-Nitrobenzyl)-phthalimide.**—*p*-Nitrobenzyl bromide was heated with potassium phthalimide according to Ing and Manske.[25] A 46% yield of N-(*p*-nitrobenzyl)-phthalimide was obtained, m. p. 165–166°; lit. m. p. 174–175°.[26]

Anal. Calcd. for $C_{15}H_{10}N_2O_4$: N, 9.92. Found: N, 9.64.

(b) **N-(*p*-Aminobenzyl)-phthalimide.**—Catalytic reduction of N-(*p*-nitrobenzyl)-phthalimide along the lines employed for the meta isomer gave N-(*p*-aminobenzyl)-phthalimide. This, after recrystallization from aqueous ethanol, melted at 197–198°; lit. m. p. 187–188°[24]; yield 65%.

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: N, 11.11 Found: N, 10.85.

(c) ***p*-Aminobenzylamine.**—N-(*p*-Aminobenzyl)-phthalimide was hydrolyzed with hydrazine hydrate in the usual way.[25] A 48% yield of *p*-aminobenzylamine was obtained; b. p. 142–143° (10 mm.); lit. value, b. p. 268–270°[27]; $n^{20}D$ 1.6095.

Anal. Calcd. for $C_7H_{10}N_2$: N, 22.95; Found: N, 22.51, 22.54.

The dibenzoyl derivative melts at 212–213°.

Anal. Calcd. for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.50. Found: C, 76.18; H, 5.55.

Preparation of β-(*o*-Aminophenyl)-ethylamine. (a) ***o*-Nitrobenzyl Bromide.**—A mixture of 196 g. of N-bromosuccinimide,[28] 196 g. of *o*-nitrotoluene, and 1.5 g. of dibenzoyl peroxide was placed in 350 ml. of carbon tetrachloride and refluxed for twelve hours with stirring. The product was cooled to 5° and the precipitate of succinimide and N-bromosuccinimide removed by filtration. The filtrate was heated on a steam cone until no more carbon tetrachloride came over following which the residue was washed successively with 15% aqueous sodium bisulfite, water, 15% aqueous ferrous sulfate and water. It was than dried over anhydrous sodium sulfate and treated with decolorizing carbon. The product was divided into two equal portions and the residual carbon tetrachloride and unreacted *o*-nitrotoluene was removed by distillation at 1 to 2 mm. (b. p. *ca.* 70–80°); *the bath temperature was maintained below 125°*. It is imperative that this distillation be conducted at as low a temperature as possible since in two instances distillation at 5 mm. and a bath temperature greater than 125° resulted in violent decomposition. On the other hand, this distillation has been carried out many times under the specified conditions without difficulty. The recovered *o*-nitrotoluene amounted to 57% of the starting material.

The undistilled residue was extracted repeatedly with boiling petroleum ether (b. p. 30–60°). The *o*-nitrobenzyl bromide which crystallized on cooling the extracts was isolated and washed with cold petroleum ether. A total of 69 g. was obtained (this corresponds to a 51% yield if the recovery of *o*-nitrotoluene is taken into account). This *o*-nitrobenzyl bromide, which melted at 44–46°, was used without further purification; lit. m. p.[29] 45.8–46.3°.

(b) ***o*-Nitrohydrocinnamic Acid.**—This compound was prepared according to Jaenish[30] with the exception that *o*-nitrobenzyl bromide was used instead of *o*-nitrobenzyl chloride. The product was recrystallized from water; yield 29%; m. p. 113–114°, lit.[30] m. p. 115°.

(c) **β-(*o*-Nitrophenyl)-ethylamine.**—Seven grams (0.036 mole) of *o*-nitrohydrocinnamic acid was dissolved in 17 ml. of 96% sulfuric acid and stirred at 40–45° with 37 ml. of a chloroform–hydrazoic acid solution[14] containing 0.043 mole of hydrazoic acid. When the evolution of nitrogen had stopped the chloroform layer was decanted and the sulfuric acid phase was poured over 100 g. of ice. This acid solution was made strongly alkaline with 25% aqueous sodium hydroxide and continuously ether extracted. The extract was dried with anhydrous sodium sulfate, concentrated and vacuum distilled. Four and nine-tenths grams of β-(*o*-nitrophenyl)-ethylamine was obtained (83% yield); b. p. 135–136° (5 mm.); $n^{20}D$ 1.5635; lit. value,[30] b. p. 147° (13 mm.).

The benzoyl derivative melts at 94–95°; Jaenish[30] reports m. p. 98°.

(d) **β-(*o*-Aminophenyl)-ethylamine.**—Four and six-tenths grams of β-(*o*-nitrophenyl)-ethylamine was dissolved in 50 ml. of absolute ethyl alcohol and reduced by shaking with Raney nickel and hydrogen at 3 atm. Decolorizing charcoal was added and the reaction mixture was filtered. The pale yellow filtrate was treated with 5 ml. of 37% hydrochloric acid and the alcohol was removed by heating on a steam cone. The sirup which remained was dissolved in 50 ml. of water, made alkaline with excess 25% aqueous sodium hydroxide and continuously ether extracted. The ether extract was dried over potassium hydroxide, concentrated and vacuum distilled. An 82% yield of β-(*o*-aminophenyl)-ethylamine was obtained; b. p. 112–113° (2 mm.); $n^{20}D$ 1.5960.

Anal. Calcd. for $C_8H_{12}N_2$: N, 20.57. Found: N, 20.50.

The dibenzoyl derivative melts at 139–140°; lit.[30] m. p. 139–140°.

Preparation of β-(*m*-Aminophenyl)-ethylamine. (a) ***m*-Benzoylaminohydrocinnamic Acid.**—Ten grams (0.052 mole) of *m*-nitrocinnamic acid[31] was suspended in 100 ml. of absolute ethanol and 5 g. (wet weight) of Raney nickel was added. Hydrogenation at 3 atm. resulted in uptake of the amount of hydrogen necessary to reduce the nitro group to an amino group. The nickel was filtered off, 0.2 g. of Adams catalyst was added, and the hydrogenation continued until the double bond was saturated. After filtration, the ethanol solution was concentrated on a steam-bath, the residue was dissolved in excess 10% aqueous sodium hydroxide, and 7.3 g. of benzoyl chloride was added. The mixture was shaken vigorously until it became homogeneous whereupon it was acidified with cold 20% sulfuric acid. The crude *m*-benzoylaminohydrocinnamic acid which separated was recrystallized twice from aqueous ethanol; yield 6.8 g. (50%); m.p. 146–148°. lit. value,[32] m. p. 149°.

(b) **β-(*m*-Aminophenyl)-ethylamine.**—Twelve and a half grams (0.047 mole) of *m*-benzoylaminohydrocinnamic acid was dissolved in 30 ml. of cold 96% sulfuric acid. While stirring, 40 ml. of a chloroform solution containing 0.055 mole of hydrazoic acid[14] was added dropwise, keeping the temperature below 45°. After complete addition of the chloroform solution stirring was continued and the mixture was maintained between 40 to 45° until the evolution of nitrogen ceased (about three hours). The chloroform was decanted and the sulfuric acid layer carefully diluted with 60 ml. of water. The aqueous solution was then heated eight hours on a steam-bath; benzoic acid separated as the hydrolysis proceeded. At the end of the hydrolysis the solution was made alkaline and continuously extracted with ether. The extract was dried with potassium hydroxide, concentrated and vacuum distilled to produce 4.8 g. of β-(*m*-aminophenyl)-ethylamine; yield, 75%; b. p. 138–139° (4 mm.); $n^{20}D$ 1.5930; lit. value,[32] b. p. 156–157° (21 mm.).

Anal. Calcd. for $C_8H_{12}N_2$: N, 20.57. Found: N, 20.62.

The dibenzoyl derivative melts at 174–175°; lit. value,[32] m.p. 176°.

Preparation of β-(*p*-Aminophenyl)-ethylamine.—A suspension of 16.2 g. of *p*-nitrophenylacetonitrile in 75 ml. of acetic anhydride was reduced in the same manner as *o*-nitrobenzonitrile (see above). However, the amorphous

(26) Salkowski, *Ber.*, **22**, 2142 (1889).
(27) Amsel and Hofmann, *ibid.*, **19**, 1288 (1886).
(28) Ziegler, *et al.*, *Ann.*, **551**, 80 (1942).
(29) Sprung, THIS JOURNAL, **52**, 1643 (1930).
(30) Jaenish, *Ber.*, **56**, 2448 (1923).
(31) Thayer, "Organic Syntheses," Col. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1941, p. 398.
(32) Fries and Bestian, *Ann.*, **533**, 72 (1937).

precipitate formed after removing the catalyst and rendering the filtrate alkaline was hydrolyzed by refluxing for ten hours with 30 ml. of 37% hydrochloric acid; 4.0 g. (30% yield) of undistilled diamine was obtained.

Three and a half grams of the crude product was vacuum distilled; b.p. 150–152° (19 mm.); yield 2.87 g. of a colorless liquid. Upon cooling in ice this liquid solidified; on warming it melted between 25–30°. In the hope that further purification would raise the melting point, 2.7 g. of the liquid was converted to the diacetyl derivative. After recrystallization from a mixture of ethanol and benzene 4 g. of the diacetyl derivative was obtained; m.p. 190–191°, lit. value,[33] 190–192°. This diacetyl derivative was dissolved in 30 ml. of 12% hydrochloric acid and heated ten hours on a steam-bath. The β-(*p*-aminophenyl)-ethylamine was then isolated as described above. Two and one-tenth grams of diamine, b.p. 150° (9 mm.), was obtained; it solidified upon standing at room temperature; m.p. 28–31°.

Anal. Calcd. for $C_8H_{12}N_2$: N, 20.57. Found: N, 20.82.

Preparation of 1-(*p*-Aminophenyl)-5-aminopentane.[34] (a) **Ethyl Hydrogen Adipate.**—The directions for preparing ethyl hydrogen sebacate[35] were used; yield 65%; b.p. 152–154° (3 mm.); lit. value,[35] b.p. 155–157° (7 mm.)

(b) **δ-Carbethoxypentanoyl Chloride.**—This was obtained from ethyl hydrogen adipate by treatment with thionyl chloride[36]; b.p. 122–124° (15 mm.), lit. b.p.[37] 128° (17 mm.).

(c) **5-Benzoylpentanoic Acid.**—Following the method of Cason[38] a solution of diphenylcadmium in benzene was prepared from 66 g. of bromobenzene. To this a solution of 40 g. of δ-carbethoxypentanoyl chloride in 50 ml. of benzene was added in about fifteen minutes while the mixture was vigorously stirred and refluxed. The reaction mixture was stirred and refluxed for an additional half-hour and then cooled and poured into a cold solution of 200 ml. of water and 50 ml. of concentrated sulfuric acid. The benzene phase was separated and the benzene removed by steam distillation. The residue was refluxed for fifteen hours with a mixture of 200 g. of 25% aqueous sodium hydroxide and 170 ml. of 95% ethanol. After removing the ethanol by distillation the solution was acidified with sulfuric acid; the oil thus produced crystallized on standing overnight. Recrystallization from aqueous ethanol gave 29.5 g. of material melting from 69–71°. This was dissolved in 100 ml. of warm water containing 2 equivalents of sodium hydroxide and extracted with benzene. Reacidification followed by recrystallization from a mixture of benzene and petroleum ether gave 27 g. (64% yield) of 5-benzoylpentanoic acid; m.p. 76–77°; lit.[39] m.p. 78°.

(d) **6-Phenylhexanoic Acid.**—Clemmensen reduction[40] of 5-benzoylpentanoic acid gave 6-phenylhexanoic acid in 85% yield; b.p. 149–150° (1 mm.); $n^{25}D$ 1.5173; lit.[41] b.p. 206–208° (30 mm.).

(e) **6-(*p*-Nitrophenyl)-hexanoic Acid.**—Nitration of 6-phenylhexanoic acid at 25–30°[42] gave a crude product which, on standing four days at 0°, deposited crystals of 6-(*p*-nitrophenyl)-hexanoic acid. These were separated from oily impurities by filtration and recrystallized from a mixture of benzene and petroleum ether. A 19% yield of material melting at 60–63° was obtained. A small portion, after further recrystallization from benzene-petroleum ether melted at 65–66°; lit. m.p.[42] 64–65°.

(f) **6-(*p*-Aminophenyl)-hexanoic Acid.**—Hydrogenation at three atmospheres pressure of 6-(*p*-nitrophenyl)-hexanoic acid (m.p. 60–63°) in 95% ethanol solution over Adams catalyst gave 6-(*p*-aminophenyl)-hexanoic acid in 75% yield; m.p. 105–107°. Recrystallization from hot water raised the m. p. to 107–108°; Van der Scheer[42] reports m. p. 108–109°.

(g) **1-(*p*-Aminophenyl)-5-aminopentane.**—Conversion of 6-(*p*-aminophenyl)-hexanoic acid (m. p. 105–107°) to 1-(*p*-aminophenyl)-5-aminopentane was effected in 55% yield by the Schmidt reaction[14]; b. p. 149–150° (1 mm.). A 150-mg. sample was redistilled for analysis; $n^{25}D$ 1.5437. On standing at 0° this diamine crystallized, m. p. 33–35°.

Anal. Calcd. for $C_{11}H_{18}N_2$: N, 15.72. Found: N, 15.52, 15.62.

The dibenzoyl derivative, after recrystallization from aquoeus ethanol, melts at 148–148.5°.

Anal. Calcd. for $C_{25}H_{26}N_2O_2$: N, 7.25. Found: N, 7.34.

Attempted Selective Deamination of *o*-Aminobenzylamine. (a) **According to Procedure I.**—When 1.22 g. of *o*-aminobenzylamine was subjected to procedure I, evolution of nitrogen took place for *ca.* one-half hour and then ceased. After twenty-four hours, the starch-iodide test for nitrous acid was negative and diazonium ions were absent (*no* coupling with alkaline β-naphthol). The reaction mixture was extracted with four 10-ml. portions of ether and these were washed with 10% aqueous sodium hydroxide and water. After drying with anhydrous sodium sulfate the ether was removed leaving 0.1 g. of a brown residue which was vacuum distilled at 10 mm. The benzyl alcohol thus obtained had $n^{25}D$ 1.5382; lit. value[43] $n^{25}D$ 1.5387, and its 3,5-dinitrobenzoate melted at 111–113°. The accepted m. p. of the benzyl ester of 3,5-dinitrobenzoic acid is 112°.[44]

The aqueous solution from which the benzyl alcohol had been extracted was made alkaline and continuously ether extracted. The extract was dried over sodium hydroxide and then concentrated; the viscous residue weighed 0.45 g. It was alkaline to moist litmus, had the musty acetamide-like odor characteristic of *o*-aminobenzylamine, and gave a positive test for arylamine.[45] There was not a trace of the sharp odor of benzylamine.

(b) **Using Excess Sodium Nitrite.**—One gram (0.0084 mole) of *o*-aminobenzylamine was dissolved in 5.6 g. of 50% aqueous hypophosphorous acid (0.042 mole) and diluted with 5.6 ml. of water; this is solution A. A second solution, B, was prepared by adding a cold solution of 3.0 g. (0.042 mole) of sodium nitrite in 11 ml. of water to 10.2 g. of cold 50% aqueous hypophosphorous acid. Solution B was covered with 6 ml. of a 1:1 mixture of 30–60° petroleum ether and benzene and then solution A was slowly added, with stirring, while the reaction temperature was maintained between 0 to 5°. After one-half hour 1.2 g. more of sodium nitrite in 3 ml. of water was added and then the mixture was stirred at room temperature until the test for diazonium ions was negative (forty-eight hours).

The reaction mixture was extracted with benzene, dried over sodium sulfate, and then heated on the steam-bath to remove solvents. The brown residual liquid weighed 0.5 g. and upon distillation at 10 mm. pressure it yielded a colorless sample of benzyl alcohol, $n^{25}D$ 1.5370. The 3,5-dinitrobenzoate melted at 111–112° and a mixed m. p. with an authentic sample was undepressed.

The acid reaction mixture was made alkaline and exhaustively extracted with ether. After distilling away the ether a small residue was obtained which gave a positive test for arylamine[45] and had none of the characteristic odor of benzylamine.

(c) **Using Excess Sodium Nitrite in the Presence of Hydrochloric Acid.**—To a solution of 1.83 g. (0.015 mole)

(33) Maron, German Patent 294,085; *Chem. Centr.*, **87**, II, 706 (1916).

(34) Carried out at the University of West Virginia.

(35) Swann, Oehler and Buswell, "Organic Syntheses," Col. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 276.

(36) Cason, "Organic Syntheses," **25**, 21 (1945); see especially note 12.

(37) Blaise and Koehler, *Bull. soc. chim.*, [4] **7**, 219 (1910).

(38) Cason, THIS JOURNAL, **68**, 2078 (1946).

(39) Auwers and Treppman, *Ber.*, **48**, 1217 (1915).

(40) Martin, "Organic Syntheses," Col. Vol. II, p. 499 (1943).

(41) Borsche, *Ber.*, **52**, 2084 (1918).

(42) Van der Scheer, THIS JOURNAL, **56**, 744 (1934).

(43) Walden, *Z. physik. Chem.*, **59**, 395 (1907).

(44) Shriner and Fuson "Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 3rd ed., 1948, p. 227.

(45) Ref. 44, p. 113.

of *o*-aminobenzylamine in 10 g. (0.075 mole) of 50% hypophosphorous acid was added 10 ml. of water (solution A). Solution B was made up by mixing a cold solution of 5.4 g. (0.075 mole) sodium nitrite in 15 ml. of water and 20 g. of cold 50% hypophosphorous acid (0.15 mole). Solution B was cooled to −5 to 0° and, with stirring, solution A was slowly added simultaneously with 9 ml. of 15% aqueous hydrochloric acid (0.045 mole).

After an hour at 0° the reaction mixture was permitted to come to room temperature and stand for twelve hours. The product was extracted with four 5-ml. portions of ether and these were washed with 5% aqueous sodium hydroxide, with water and then dried over anhydrous sodium sulfate. The solvent was removed on a steam-bath and the residue vacuum distilled. One gram of benzyl chloride was obtained; the colorless product boiled at 80° (8 mm.); $n^{20}D$ 1.5373; lit. value[46] $n^{20}D$ 1.5391. The benzyl chloride thus obtained gave a positive Beilstein test and did not give a 3,5-dinitrobenzoate upon treatment with 3,5-dinitrobenzoyl chloride. In contrast, a 50-mg. sample when refluxed for two hours in dry benzene containing dry silver 3,5-dinitrobenzoate gave the ester; m. p. and mixed m. p. with authentic benzyl 3,5-dinitrobenzoate, 112–113°.

The acid reaction mixture from which the benzyl chloride had been extracted was made alkaline and exhaustively extracted with ether. Removal of the solvent yielded one drop of brown residue which gave a negative arylamine test and did not have an amine odor.

Attempted Reaction of Benzylamine with Nitrous Acid. (a)—To 660 g. of 25% aqueous hypophosphorous acid (2.5 moles) was added 21.4 g. (0.2 mole) of benzylamine. The solution was cooled to 0° and, while stirring, 21.5 g. (0.3 mole) of 97% sodium nitrite was added. After fifteen hours at 0° and twenty-four hours at room temperature the reaction product was extracted with four 60-ml. portions of ether. These extracts were combined, dried over sodium sulfate, and concentrated on a steam-bath. The few drops of brown liquid which remained were soluble in concentrated sulfuric acid, gave a negative ceric nitrate test[47] for alcohols, and a negative fuchsin-aldehyde test.

The aqueous layer was made alkaline and extracted with four 100-ml. portions of ether. These were combined, dried over potassium hydroxide, concentrated and the residue vacuum distilled. A 92% recovery of benzylamine was obtained; 19.7 g., b. p. 41–42° (4 mm.); $n^{20}D$ 1.5424.

Experiments employing 50, 35 and 15% aqueous hypophosphorous acid also failed to give either toluene or benzyl alcohol. Instead, benzylamine was recovered in 90–93% yield.

(b)—When 8.0 g. of benzylamine was subjected to the conditions described in part c of the "Attempted Selective Deamination of *o*-Aminobenzylamine," 7.1 g. (89%) was recovered; b. p. 179–181°.

Deamination of *o*-Aminobenzyl Alcohol[11] (a)—Upon treating 1 g. of *o*-aminobenzyl alcohol in the manner described in part a of the "Attempted Selective Deamination of *o*-Aminobenzylamine," 0.47 g. (54% yield) of benzyl alcohol was obtained; $n^{20}D$ 1.5388; lit. value[43] $n^{25}D$ 1.5387. The 3,5-dinitrobenzoate had m. p. and mixed m. p. 110–112°.

(b)—When 5 g. of *o*-aminobenzyl alcohol was deaminated according to part b of the "Attempted Selective Deamination of *o*-Aminobenzylamine," 1.95 g. (45% yield) of benzyl alcohol was produced; $n^{20}D$ 1.5399. The 3,5-dinitrobenzoate melted 110–112° alone and when mixed with an authentic sample.

(46) Huntress, "Organic Chlorine Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 1160.

(47) Ref. 44, p. 96.

Summary

Aliphatic primary amines are not attacked by nitrous acid below *p*H 3. In contrast, aromatic primary amines are readily diazotized in comparatively strongly acidic solutions (*p*H below 1). Consequently, by maintaining the *p*H below 3 selective diazotization of the aromatic primary amino group is easily achieved. The resulting diazonium salts are susceptible to the usual reactions of diazonium compounds; in the present investigation replacement of the diazo group by hydrogen was accomplished by reduction with hypophosphorous acid.

The over-all result is a simple method for replacing an aromatic primary amino group by hydrogen without affecting any aliphatic amino group which may be present. The generality of this selective deamination reaction has been demonstrated by its successful application to thirteen aromatic–aliphatic diamines in which the side chains are ortho, meta and para to the aromatic amino group. The only diamine which fails to undergo the selective deamination reaction is *o*-aminobenzylamine; the reasons for this are discussed.

WEST LAFAYETTE, INDIANA

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[CONTRIBUTION OF THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Preparation of Trimethylamine-borine, N-Trimethylborazole and N-Dimethylaminoborine

BY GEORGE W. SCHAEFFER[1] AND ELAINE R. ANDERSON[2]

An investigation of the reactions of lithium borohydride and the methylammonium chlorides in ether solution has led to the development of excellent methods for the preparation of trimethylamine-borine, $(CH_3)_3N{:}BH_3$; N-dimethylaminoborine, $(CH_3)_2NBH_2$; and N-trimethylborazole, $B_3H_3N(CH_3)_3$. Previously, these compounds have been prepared by the reaction of diborane with the appropriate anhydrous amine in sealed tubes, employing high vacuum techniques. The experimental difficulties inherent in this type of reaction and the necessary limitations on the quantities of materials used, have made these substances available only in millimole quantities. By the methods described herein, these compounds can be prepared from readily available reagents, in reasonable yields, using the usual techniques of organic synthesis.

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