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Studies of Oxidation of Benzylamines with Neutral Potassium Permanganate and the Chemistry of the Products Thereof. I

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Substituted benzylamines are oxidized with potassium permanganate buffered by calcium sulfate to substituted N-[α-(benzylideneamino)-benzyl]-benzamides (I) and N,N′-(iminodibenzylidene)-bis-[benzamides] (II). The structures of these products were established by analytical and physical methods and by hydrolysis to ammonia and to their corresponding benzamides and benzaldehydes. Acetylative hydrolysis and benzoylative hydrolysis of N-[α-(benzylideneamino)-benzyl]-benzamide (III) gave N-(α-acetamidobenzyl)-benzamide (V) and N,N-benzylidenebis-[benzamide] (VI), respectively. Reduction of N-[α-(benzylideneamino)-benzyl]-benzamides (I) with sodium borohydride yielded N-[α-(dibenzylamino)-benzyl]-benzamides and N-[α-(benzylamino)-benzyl]-benzamides. Possible mechanisms of oxidation of benzylamines, of acylative hydrolysis, and of reduction of Schiff bases by sodium borohydride are discussed.

Although permanganates are among the most versatile oxidants in organic chemistry, their actions with amines have received little attention. Permanganates have been used to oxidize specific amines under a variety of conditions; however, the scope, utility, and mechanisms of such reactions have not been systematically investigated.

Primary amines are oxidized rapidly by permanganates. Ethylamine[2a] and butylamine[2b] are converted to acetaldehyde and to butyric acid by aqueous potassium permanganate; under alkaline conditions benzylamine is oxidized to benzaldehyde,[2c,d] benzoic acid,[2c,d] and benzamide.[2c] Nitrosocyclohexane and cyclohexanone oxime are obtained by oxidation of cyclohexylamine in the presence of formaldehyde[2e] or acetaldehyde[2f,3]; reactions of benzhydrylamine[2g] and 9-aminofluorene[2g] with potassium permanganate in acetone yield benzophenone imine and 9-iminofluorene, respectively.[3] *t*-Carbinamines[2h] are oxidized to the corresponding nitro compounds by permanganates.

Secondary amines such as diethylamine[2b] and N-methylpropylamine[2b] have been oxidized by permanganate to acetic acid and to formic and propionic acids, respectively. Oxidations of dibenzylamine[2d] to tribenzylbenzoylhydrazine, dipropylamine[2d] to 1,2-dipropyl-1,2-dipropionylhydrazine, and piperidine[2d] to 1,1′-bipiperidin-2-one have been reported. Acid permanganate has little action on tertiary aliphatic amines except under conditions which are so vigorous that the amines are completely disrupted. The lack of oxidizability of such amines in acid solution apparently stems from their conversion to trialkylammonium ions. Similarly, tetramethyl[2i] and tetraethylammonium[2i] salts are not affected by permanganates. Secondary and tertiary amines containing substituted benzyl groups have been oxidized by acidic potassium permanganate. The substituted benzylamino groups[2j] are oxidized to the corresponding benzaldehydes; frequently acids corresponding to the substituted benzaldehydes are produced.[2j] The N-methyl groups of such secondary and tertiary amines are reported as resistant to oxidation.[2j]

A study has been presently made of homogeneous oxidation of various substituted benzylamines with potassium permanganate in aqueous *t*-butyl alcohol. Oxidations with permanganate may be effected in many ways to yield different products depending upon which reactant is used in excess. Acids and bases affect the strength of permanganate as an oxidant as well as the conversion of an amine to its conjugate acid. Advantageous control of the oxidant and the subsequent courses and products of reaction have been effected in the present work by use of buffered permanganate. The oxidation medium is maintained essentially neutral by use of excess calcium sulfate as the buffer in that the calcium hydroxide formed during oxidation is only slightly soluble in the solvent used. The stoichiometry involving the oxidant in the presence of the buffering agent is indicated by eq. 1.

$$2KMnO_4 + CaSO_4 + H_2O \longrightarrow Ca(OH)_2 + 2MnO_2 + K_2SO_4 + 3[O] \quad (1)$$

Oxidation of representative *o*-, *m*-, and *p*-substituted benzylamines (Table I) with potassium permanganate (1.25 equivalents) and excess calcium sulfate in water–*t*-butyl alcohol (1:1) at 25–30° occurs rapidly and in satisfactory yields to give the corresponding substituted N-[α-(benzylideneamino)-benzyl]-benzamides (I)[4] and often N,N′-(iminodibenzylidene)-bis-[benzamides][4] (II) along with the benzoic acids and ammonia. Products of type I are much more soluble in nonpolar organic solvents than are those of type II and thus separation of the oxidation products can be effected with little difficulty. Because of the ease of preparation of such unusual derivatives as I and II and the varied chemistry which these products undergo, oxidation of benzylamines and related amines with per-

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[1] (a) To whom inquiries may be directed. (b) The studies of oxidation of benzylamine and its *p*-methyl, *p*-chloro, *p*-methoxy, and *p*-nitro derivatives, and the chemistry of the products thereof are abstracted in part from the Ph.D. dissertation of S. S. Rawalay, The Ohio State University, 1962. This research was sponsored primarily by the U. S. Army Research Office, Grant DA-ARO(D)-31-124-G182, ARO(D) 2367-C. (c) Subsequent studies of oxidation of other benzylamines (Table I) were effected at the University of California and the Veterans Administration Center, Los Angeles, Calif., under the sponsorship of Research Grant AM-06636-01 from the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service. (d) The technical assistance of Mr. A. K. Balla in part of this work is gratefully acknowledged.

[2] (a) E. Carstanjen, *J. prakt. Chem.*, **89**, 486 (1863); (b) O. Wallach and L. Claisen, *Ber.*, **8**, 1237 (1875); (c) K. Kindler, *Ann.*, **43**, 187 (1923); (d) S. Goldschmidt and V. Voeth, *ibid.*, **435**, 265 (1924); (e) I. Okamura, R. Sakurai, and T. Tanabe, *Chem. High Polymers* (Tokyo), **9**, 279 (1952); (f) I. Okamura and R. Sakurai, *ibid.*, **9**, 434 (1952); (g) S. Goldschmidt and W. Beuschel, *Ann.*, **447**, 197 (1926); (h) N. Kornblum, R. J. Cutter, and W. J. Jones, *J. Am. Chem. Soc.*, **78**, 4003 (1956); (i) D. Vorlander, G. Blau, and T. Wallis, *Ann.*, **345**, 251 (1906); (j) R. A. Labriola, M. Ishii, and I. Mariani, *Anales. Asoc. Quim. Argentina*, **33**, 156 (1945).

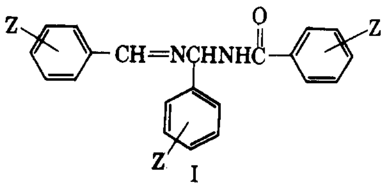
[3] Reaction of these amines with permanganate in the presence of aldehydes or ketones may actually involve oxidation of the corresponding Schiff bases or of other intermediates derived from condensation of the amines with the carbonyl reagents.

[4] The authors should like to acknowledge the advice and assistance of *Chemical Abstracts* with respect to the complex nomenclature frequently necessary in this manuscript.

TABLE I: OXIDATION OF SUBSTITUTED BENZYLAMINES WITH NEUTRAL POTASSIUM PERMANGANATE

Z-Benzylamine,[a] moles × 10^{-2}	KMnO₄, moles × 10^{-2}	CaSO₄, moles × 10^{-2}	Product of[b,c] type I, % yield	M.p., °C.	Anal., calcd. % C	Anal., calcd. % H	Anal., calcd. % N	Anal., found % C	Anal., found % H	Anal., found % N	Product of[b,d] type II, % yield	M.p., °C.	Anal., calcd. % C	Anal., calcd. % H	Anal., calcd. % N	Anal., found % C	Anal., found % H	Anal., found % N
H, 4.66	4.00	2.57	51	146–149	80.21	5.78	8.91	79.57	5.79	9.17	9	158–160	77.22	5.79	9.64	77.23	5.88	9.36
4-Methyl, 4.12	3.48	2.38	74	125–129[e]	80.87	6.79	7.85	81.06	6.97	7.67	11	140–142[f]	78.17	6.77	8.55	78.20	6.87	8.35
4-Chloro, 3.52	2.85	2.02	75	154–157[g]	60.31	3.63	6.69	60.20	3.75	6.81	10	171–173[h]	58.65	3.66	7.35	58.85	3.56	7.56
4-Methoxy, 3.64	3.00	1.74	89	130–133[i]	71.27	5.98	6.94	71.34	5.97	7.15								
4-Nitro,[j] 1.24[j]	2.15	1.45	46	153–156[k,l]	56.14	3.37	15.59	56.41	3.54	15.38	10	184–186	54.64	3.43	15.91	54.79	3.76	5.52
4-Fluoro, 3.96	3.33	2.30	57	142–145[m]	68.47	4.11	7.60	68.76	4.23	7.57								
3-Methyl, 4.12	3.48	2.30	62	133–136[n]	80.87	6.79	7.85	80.80	6.66	8.04	10	137–139	78.17	6.77	8.55	78.61	6.69	8.54
2-Methyl, 4.12	3.48	2.30	78	116–118[o]	80.87	6.79	7.85	80.92	6.68	8.13								
2-Chloro, 3.52	2.85	1.74	84	145–148[p]	60.31	3.63	6.69	60.46	3.91	7.03								
2,4-Dimethyl, 3.70	3.00	1.74	66	176–176[q]	81.38	7.59	7.03	81.57	7.28	7.09								
2,5-Dimethyl, 3.70	3.00	1.74	45	139–142[r]	81.38	7.59	7.03	81.17	7.31	7.26								
3,4-Dimethyl, 3.70	3.00	1.74	42	121–124[s]	81.38	7.59	7.03	81.06	7.61	7.12								
2,4-Dichloro, 2.84	2.37	1.45	49	173–175	48.41	2.32	5.38	48.64	2.13	5.45								
3,4-Dichloro, 2.37	2.37	1.45	47	166–170	48.41	2.32	5.38	48.69	2.53	5.65								

[a] All oxidations were effected by adding the benzylamine in one portion to the oxidant in 50 ml. of *t*-butyl alcohol and 50 ml. of water. [b] Molecular weights were determined using a Mechrolab vapor pressure osmometer, Model 301A using 1,2-dichloroethane, benzene, or chloroform as solvents. [c] The products exhibited strong infrared absorption for NH (~3.0 μ), amide carbonyl (~6.05 μ), and C—N (~6.20 μ) groups. [d] Strong infrared absorptions for NH (~3.0 μ) and amide carbonyl (~6.05 μ) were exhibited in all cases. [e] White needles, λ_{max} 257 mμ (log ε 4.43) in 95% EtOH; mol. wt. calcd. 356, found 346. [f] White crystals; mol. wt. calcd. 492, found 479. [g] White spheres; λ_{max} 255 mμ (log ε 4.48) in 95% EtOH; mol. wt. calcd. 418, found 424. [h] Mol. wt. calcd. 573, found 557. [i] λ_{max} 275 mμ (log ε 4.57) in 95% EtOH; mol. wt. calcd. 404, found 390. [j] Prepared as its sulfate (m.p. 230–232°. *Anal.* Calcd. for $C_{14}H_{18}N_4O_8S$: N, 13.93. Found: N, 14.06) by reaction of *p*-nitrophenylacetic acid and hydrazoic acid in concentrated sulfuric acid. [k] Yellow crystals, λ_{max} 269 mμ (log ε 4.56) in 95% EtOH; mol. wt. calcd. 449, found 442. [l] *p*-Nitrobenzoic acid (m.p. and mixture m.p. 240–241°) was also obtained in 13% yield. [m] λ_{max} 246 mμ (log ε 4.23) in 95% EtOH. [n] λ_{max} 238 mμ (log ε 4.13) in 95% EtOH. [o] λ_{max} 253 mμ (log ε 4.15) in 95% EtOH. [p] λ_{max} 252 mμ (log ε 4.20) in 95% EtOH. [q] λ_{max} 260 mμ (log ε 4.38) in 95% EtOH. [r] λ_{max} 256 mμ (log ε 4.30) in 95% EtOH. [s] λ_{max} 248 mμ (log ε 4.33) in 95% EtOH.



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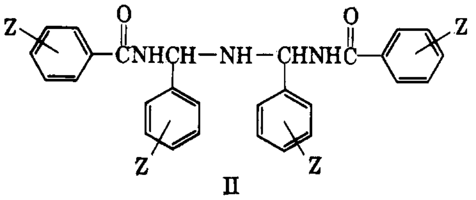
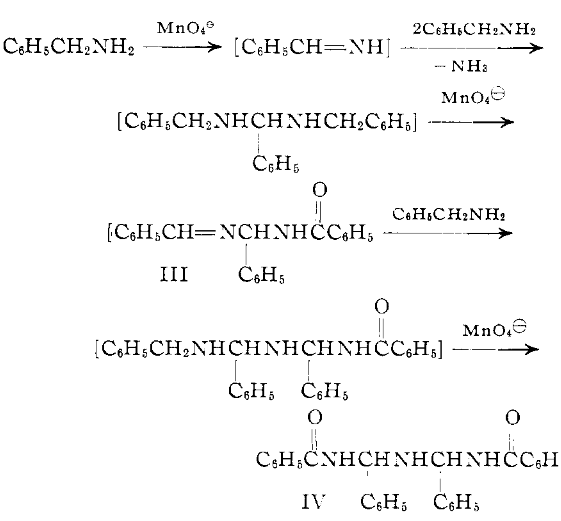


II

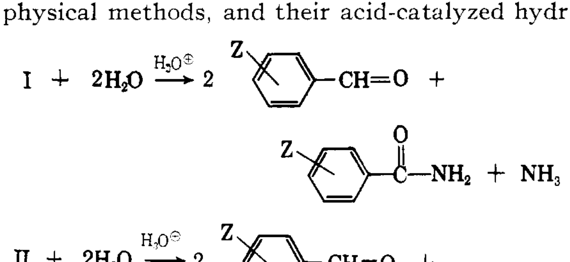
manganate offers promise as a valuable synthetic method.

The mechanisms of oxidation of benzylamines to complex products of types I and II are unknown. It is apparent, however, that oxidation of benzylamines yields benzalimines which undergo rapid addition of the parent benzylamines to give intermediates which are precursors of I and II. One of the many possible sequences for formation of products of types I and II is illustrated for benzylamine in eq. 2. It is also apparent that oxidation of a benzylamine to its benzoic acid by permanganate involves complex processes.



$$C_6H_5CH_2NH_2 \xrightarrow{MnO_4^{\ominus}} [C_6H_5CH{=}NH] \xrightarrow[-NH_3]{2C_6H_5CH_2NH_2} [C_6H_5CH_2NH\underset{C_6H_5}{CH}NHCH_2C_6H_5] \xrightarrow{MnO_4^{\ominus}} \underset{\text{III}}{[C_6H_5CH{=}N\underset{C_6H_5}{CH}NH\overset{O}{\overset{\|}{C}}C_6H_5} \xrightarrow{C_6H_5CH_2NH_2} [C_6H_5CH_2NH\underset{C_6H_5}{CH}NH\underset{C_6H_5}{CH}NH\overset{O}{\overset{\|}{C}}C_6H_5] \xrightarrow{MnO_4^{\ominus}} \underset{\text{IV}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}NH\underset{C_6H_5}{CH}NH\overset{O}{\overset{\|}{C}}C_6H_5} \quad (2)$$

The structures of products of type I were established from their analyses, molecular weights, and absorption spectra (see Experimental), by their rapid and near-quantitative hydrolyses (eq. 3) in acid solution to *p*-substituted benzaldehydes (2 equiv.), *p*-substituted benzamides (1 equiv.), and ammonia (1 equiv.), and by their many chemical transformations to recognizable products. Similarly, the structures of products of type II were assigned on the basis of analytical data, physical methods, and their acid-catalyzed hydrolyses



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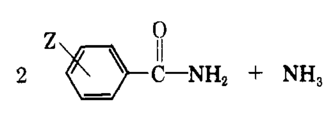
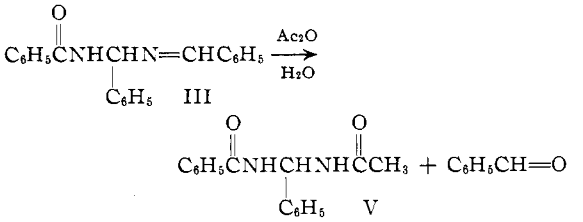
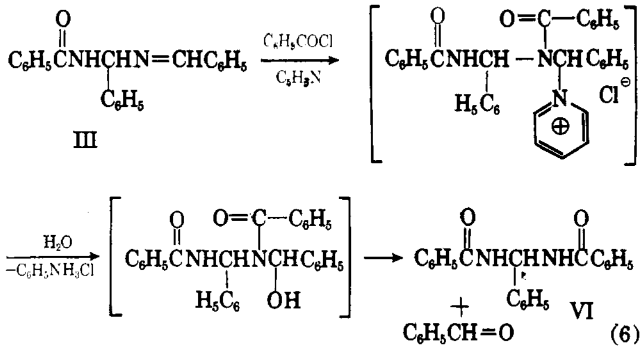


(4)

(eq. 4) to *p*-substituted benzamides (2 equiv.), *p*-substituted benzaldehydes (2 equiv.), and ammonia (1 equiv.).

A study has been made of acylation and hydrolysis of products of type I. Acetylative hydrolysis of N-[α-(benzylideneamino)-benzyl]-benzamide (III) in cold hydrochloric acid was effected by acetic anhydride and sodium acetate to yield N-(α-acetamidobenzyl)-benzamide (V, eq. 5, >79% yield) and benzaldehyde. Reaction of III in pyridine with benzoyl chloride, followed by addition of water, gave N,N′-benzylidene-bis-[benzamide] (VI, 68%) and benzaldehyde (25%). A possible sequence for transformation of III to VI is indicated in eq. 6. The structure of VI was confirmed from its analysis, molecular weight, infrared spectra, and its hydrolysis to benzamide (90%) and benzaldehyde (91%) with hydrochloric acid according to the stoichiometry of eq. 7.


$$\underset{\text{III}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}N{=}CHC_6H_5} \xrightarrow[H_2O]{Ac_2O} \underset{\text{V}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}NH\overset{O}{\overset{\|}{C}}CH_3} + C_6H_5CH{=}O \quad (5)$$



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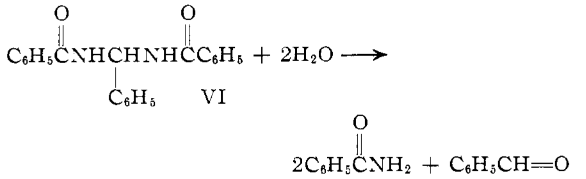
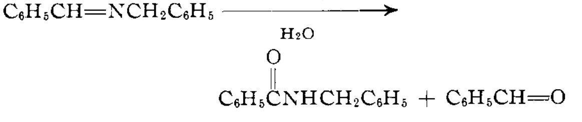
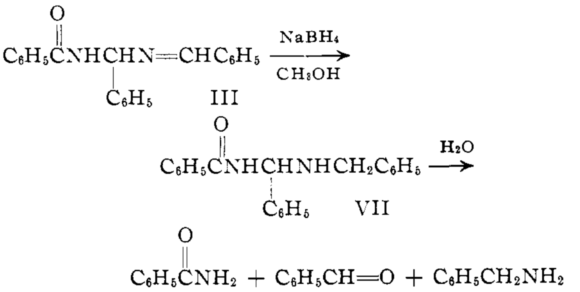

$$\underset{\text{VI}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}NH\overset{O}{\overset{\|}{C}}C_6H_5} + 2H_2O \longrightarrow 2C_6H_5\overset{O}{\overset{\|}{C}}NH_2 + C_6H_5CH{=}O \quad (7)$$

Survey of the literature did not reveal any examples of acylative hydrolysis of Schiff bases by the method of eq. 6. To test the generality of the method, N-benzylideneaniline, N-benzylidenebenzylamine (eq. 8), and N-diphenylmethyleneaniline were each treated with benzoyl chloride and pyridine and then diluted with water. Since N-phenylbenzamide (>78%), N-benzylbenzamide (>75%), and N-phenylbenzamide (>71%) were produced along with the corresponding aldehyde or ketone, the method appears reliable and offers promise for use in degradation or synthesis.

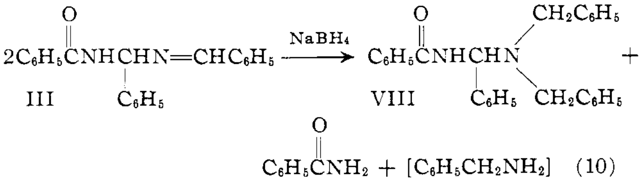

$$C_6H_5CH{=}NCH_2C_6H_5 \xrightarrow[H_2O]{C_6H_5COCl,\ C_5H_5N} C_6H_5\overset{O}{\overset{\|}{C}}NHCH_2C_6H_5 + C_6H_5CH{=}O \quad (8)$$

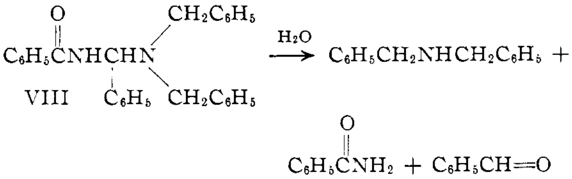
Since products of type I contain imine groups, it was of interest to investigate their reduction in some detail. Reduction of Schiff bases of the N-benzylideneaniline type with sodium borohydride yields the corresponding N-benzylanilines.[5] This method with minor modifications has been employed for selective reduction of the more complex Schiff bases of the present work. It has been found that reduction of the N-benzylidene derivatives of type I with sodium borohydride may give the simple reduction product (a secondary amine) or a more complex product (a tertiary amine) depending on the nature of the substrate or the experimental conditions.

Addition of an equimolar solution of III in methanol to a solution of sodium borohydride in methanol gave N-[α-(benzylamino)-benzyl]-benzamide (VII, 73%; eq. 9), the anticipated reduction product.


$$\underset{\text{III}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}N{=}CHC_6H_5} \xrightarrow[CH_3OH]{NaBH_4} \underset{\text{VII}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}NHCH_2C_6H_5} \xrightarrow{H_2O} C_6H_5\overset{O}{\overset{\|}{C}}NH_2 + C_6H_5CH{=}O + C_6H_5CH_2NH_2 \quad (9)$$

The structure of VII was established from its analysis, infrared absorption, and hydrolysis to benzamide (91%), benzaldehyde (90%), and benzylamine as illustrated in eq. 9. On addition, however, of powdered sodium borohydride to an equimolar solution of III in absolute methanol, N-[α-(dibenzylamino)-benzyl]-benzamide (VIII, 84%) and benzamide (82%, eq. 10) were obtained. Assignment of the structure of VIII was based on analytical data, physical methods, and its hydrolysis (eq. 11) to dibenzylamine (89%), benzamide (94%), and benzaldehyde (93%).


$$2\underset{\text{III}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}N{=}CHC_6H_5} \xrightarrow{NaBH_4} \underset{\text{VIII}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}N(CH_2C_6H_5)_2} + C_6H_5\overset{O}{\overset{\|}{C}}NH_2 + [C_6H_5CH_2NH_2] \quad (10)$$


$$\underset{\text{VIII}}{C_6H_5\overset{O}{\overset{\|}{C}}NH\underset{C_6H_5}{CH}N(CH_2C_6H_5)_2} \xrightarrow{H_2O} C_6H_5CH_2NHCH_2C_6H_5 + C_6H_5\overset{O}{\overset{\|}{C}}NH_2 + C_6H_5CH{=}O \quad (11)$$

Reduction of the Schiff bases: *p*-chloro-N-[*p*-chloro-α-[(*p*-chlorobenzylidene)-amino]-benzyl]-benzamide (IX, type I, Z = *p*-Cl) and *p*-nitro-N-[*p*-nitro-α-[(*p*-nitrobenzylidene)-amino]-benzyl]-benzamide (X, type I, Z = *p*-NO$_2$) occurred normally with sodium borohydride by either direct or inverse addition to give only the corresponding N-[α-(benzylamino)-benzyl]-benzamides (secondary amines analogous to VII). Sodium borohydride reduction of N-[*p*-methyl-α-[(*p*-methylbenzylidene)-amino]-benzyl]-*p*-toluamide (XI, type I, Z = *p*-CH$_3$) and of N-[*p*-methoxy-α-[(*p*-methoxybenzylidene)-amino]-benzyl]-*p*-anisamide (XII, type I, Z = *p*-OCH$_3$), however, gave only N-[α-(dibenzylamino)-benzyl]-benzamides (tertiary amines analogous to VIII) irrespective of the order of addition of reagents. The fact that Schiff bases of type I which contain electron-donating substituents (*p*-methyl, *p*-methoxy) give tertiary amines on reduction whereas those which

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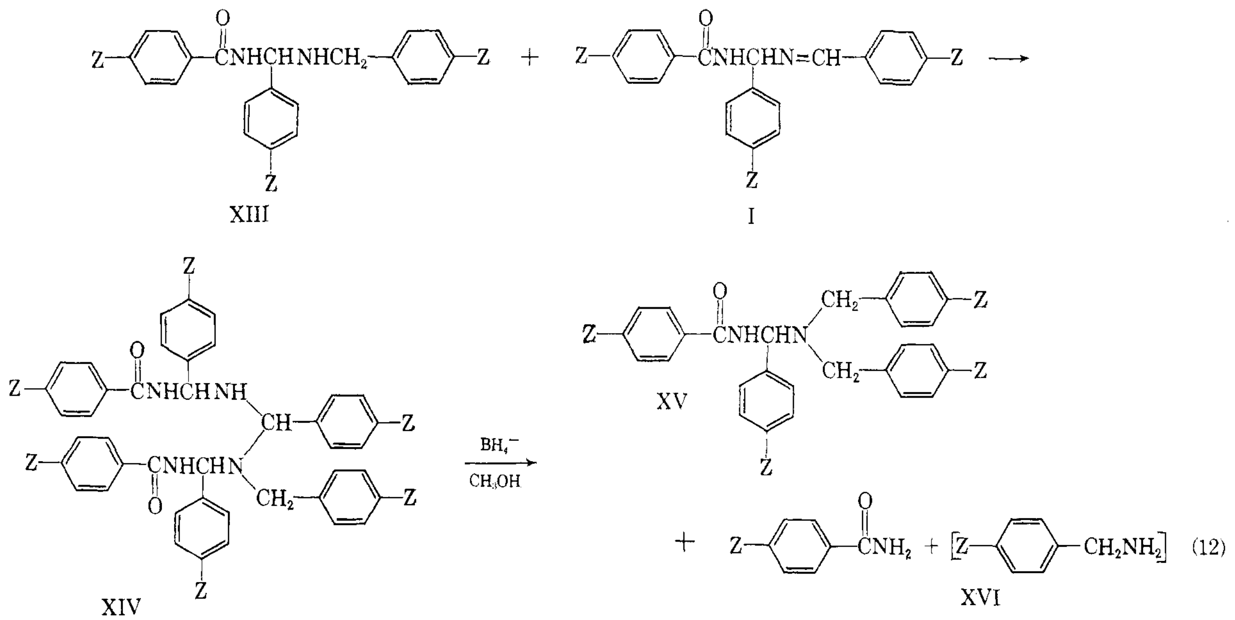
[5] J. H. Billman and A. C. Diesing, *J. Org. Chem.*, **22**, 1068 (1957); R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. V. Daeniker, and K. Schenker, *J. Am. Chem. Soc.*, **76**, 4749 (1954).



contain electron-withdrawing groups (*p*-chloro, *p*-nitro) give secondary amines is indeed striking.

The sequence of reactions and the factors involved in formation of secondary or tertiary amines by reduction of Schiff bases of type I have not been established. The results may be tentatively rationalized on the basis that reduction of I yields the corresponding secondary amines XIII and that the secondary amines XIII may undergo additions to the parent Schiff bases I to give intermediates of types XIV which are subsequently reduced and cleaved to the tertiary amines XV, the benzamide XVI, and the benzylamine.

Experimental

General Procedure.—In an oxidation the benzylamine was added in a single portion to a stirred mixture of potassium permanganate (~1.25 equiv.) and excess calcium sulfate (Drierite) in *t*-butyl alcohol–water (1:1 by volume) at 25–30°. The reaction is rapid and exothermic. If a product of type II is formed in appreciable quantity, it usually began to precipitate as reaction proceeded. The oxidations were completed within 5–15 min. Products of type II are usually stable white solids which separate readily from ether and related solvents. Products of type I are white solids which are quite soluble in ether. These products are less stable on storage and are not as sharp melting as those of II. A typical procedure for effecting an oxidation is described for benzylamine. Details and the results of oxidation of the various benzylamines of this study are summarized in Table I.

Oxidation of Benzylamine.—Benzylamine (5.0 g., 0.0466 mole) was poured into a stirred mixture of *t*-butyl alcohol (50 ml.), potassium permanganate (6.25 g., 0.04 mole, 1.25 equiv.), calcium sulfate (3.5 g., 0.0257 mole), and water (50 ml.) at 25°. As the exothermic reaction proceeded, a white solid began to appear at the liquid surface. After 0.25 hr. the mixture was cooled in ice and triturated with ether. The ether-insoluble product, N,N′-(iminodibenzylidene)-bis-[benzamide] (IV, Table I), remained as a white suspension and was filtered, washed with water, dried, and crystallized from benzene as white pyramids; yield 0.46 g. (9%); mol. wt. calcd. 435.5, found 429; strong infrared absorption for NH at 2.98 μ and for amide carbonyl at 6.07 μ.

The ether filtrate was washed with water and evaporated to give N-[α-(benzylideneamino)-benzyl]-benzamide (III, Table I) as white fluffy crystals; yield 2.5 g. (51%), λ_{max} 248 mμ (log ε 4.35) in 95% ethanol; mol. wt. calcd. 314.4, found 299; strong infrared absorption at 3.05 (NH), 6.07 (amide carbonyl), and 6.19 μ (C=N).

The inorganic residue (after trituration with ether) was extracted with water. The aqueous extract after acidification gave benzoic acid (1.1 g., 19.3%), m.p. 121–122°, no depression by an authentic sample.

Acid-Catalyzed Hydrolysis of III.—N-[α-(Benzylideneamino)-benzyl]-benzamide (III, 2.0 g., 0.00636 mole) was refluxed with dilute hydrochloric acid (12 ml., 25% by wt.) for 0.25 hr. The mixture was cooled and extracted exhaustively with ether. The aqueous layer gave a positive test for ammonia with Nessler reagent. The ether layer was evaporated and the residue added to sodium bisulfite reagent.[6] The bisulfite addition compound was filtered, washed with ether, and added to 2,4-dinitrophenylhydrazine solution to give benzaldehyde 2,4-dinitrophenylhydrazone (3.55 g., 0.0124 mole, 97.7%), m.p. and mixture m.p. 236–237°. The filtrate was extracted with ether; the ether extract gave benzamide (0.67 g., 0.0055 mole, 86.5%), m.p. and mixture m.p. 127–128°.

Acid-Catalyzed Hydrolysis of IV.—A mixture of N,N′-(iminodibenzylidene)-bis-(benzamide) (IV, 1.0 g., 0.0023 mole) and dilute hydrochloric acid (10 ml., 25% by wt.) was refluxed 0.25 hr. On working up the reaction mixture as described in the previous experiment, benzaldehyde 2,4-dinitrophenylhydrazone (1.216 g., 0.00424 mole, 93%), m.p. and mixture m.p. 236–237°, and benzamide (0.49 g., 0.00406 mole, 88%), m.p. 127–128°, were isolated. The reaction mixture gave a positive test for ammonia with Nessler reagent.

Acetylative Hydrolysis of III.—N-[α-(Benzylideneamino)-benzyl]-benzamide (III, 0.5 g., 0.0016 mole) was dissolved in dilute hydrochloric acid (50 ml., 5%). After the excess acid had been neutralized with 5% aqueous sodium hydroxide, the mixture was cooled to 5° and acetic anhydride (5 ml.) was added. The solution was stirred vigorously and aqueous sodium acetate trihydrate (10%, 50 ml.) then added. The solid which separated was filtered, washed, and dried. The crude N-(α-acetamidobenzyl)-benzamide (V) was crystallized from ethanol; yield 0.34 g. (79%), m.p. 211–212°, lit.[7] 206°; mol. wt. calcd. 268, found 257; strong infrared absorption at 3.03 (NH) and at 6.04 μ (amide carbonyl).

Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.05; N, 10.44. Found: C, 71.39; H, 6.07; N, 10.30.

Benzoylative Hydrolysis of III.—A mixture of N-[α-(benzylideneamino)-benzyl]-benzamide (1.0 g., 0.0032 mole), benzoyl chloride (1.0 g., 0.0071 mole), and pyridine (15 ml.) was warmed at 60–90° for 10 min. The solution was poured into 5% aqueous sodium bicarbonate (150 ml.) at 5°. The oily product solidified on standing. The mixture was filtered and the residue crystallized from ethanol to give N,N′-benzylidenebis-[benzamide] (VI) as colorless needles; yield 0.74 g. 68%; m.p. 229–230°, lit.[8] m.p. 231–232.5°; mol. wt. calcd. 330, found 318; infrared absorption at 3.0 (NH) and at 6.0 μ (amide carbonyl).

Anal. Calcd. for $C_{21}H_{18}N_2O_2$: C, 76.31; H, 5.49; N, 8.48. Found: C, 75.77; H, 5.50; N, 8.67.

The filtrate upon addition of 2,4-dinitrophenylhydrazine reagent gave benzaldehyde 2,4-dinitrophenylhydrazone; yield 0.71 g. (25%), m.p. and mixture m.p. 236–237°.

Reduction of III with Sodium Borohydride. Direct Addition.—A solution of N-[α-(benzylideneamino)-benzyl]-benzamide (III, 0.5 g., 0.0016 mole) in absolute methanol (40 ml.) was added dropwise in 0.5 hr. to a stirred solution of sodium borohydride (0.060 g., 0.0016 mole) in absolute methanol (25 ml.). After 0.75 hr. the mixture was diluted with water (225 ml.) and stored at 5°. White, crystalline N-[α-(benzylamino)-benzyl]-benzamide (VIII, eq. 9, 0.365 g., 0.0012 mole, 73%) was obtained,

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(6) The reagent was prepared by addition of ethanol (10 ml.) to an aqueous solution of sodium bisulfite (50%, 40 ml.) and subsequent filtration.

(7) J. B. Polya and T. M. Stopwood, *Rec. trav. chim.*, **70**, 269 (1951).

(8) H. Hellmann, G. Aichinger, and H. P. Wiedemann, *Ann.*, **626**, 44 (1959).

m.p. 127–129°; mol. wt. calcd. 316, found 317; infrared absorption at 3.05 (NH) and 6.05 μ (amide carbonyl).

Anal. Calcd. for $C_{21}H_{20}N_2O$: C, 79.71; H, 6.37; N, 8.85. Found: C, 79.92; H, 6.23; N, 8.63.

Hydrolysis of VII.—N-[α-(Benzylamino)-benzyl]-benzamide (VII, 0.5 g., 0.00158 mole) was hydrolyzed (eq. 9) with refluxing hydrochloric acid (8 ml., 25% by wt.) for 0.25 hr. The cooled mixture was extracted with ether. The extract yielded benzaldehyde (89.5%, isolated as its 2,4-dinitrophenylhydrazone, 0.405 g., 0.00141 mole), m.p. and mixture m.p. 236–237°, and benzamide (0.174 g., 0.00144 mole, 91%), m.p. and mixture m.p. 127–128°. The aqueous layer on basification followed by ether extraction gave benzylamine (80%) isolated as N-benzyl-N'-phenylthiourea (0.308 g., 0.00127 mole), m.p. and mixture m.p. 154–156°, lit.[9] 156°.

Reduction of III with Sodium Borohydride. Inverse Addition.—Sodium borohydride (0.240 g., 0.0064 mole) was added in one portion to N-[α-(benzylideneamino)-benzyl)-benzamide (III, eq. 10, 2.06 g., 0.0064 mole) in absolute methanol at 25°. After 0.75 hr., water (200 ml.) was introduced. The white solid which formed on addition of the water crystallized on storage at 5°. The product was filtered, washed with water, dried, and recrystallized from benzene to give N-[α-(dibenzylamino)-benzyl]-benzamide (VIII, 1.1 g., 84%) as white feathery needles, m.p. 179–181°; mol. wt. calcd. 407, found 396; infrared absorption at 2.98 (NH) and 6.05 μ (amide carbonyl).

Anal. Calcd. for $C_{28}H_{26}NO_2$: C, 82.73; H, 6.45; N, 6.89. Found: C, 82.62; H, 6.16; N, 7.02.

The aqueous filtrate yielded benzamide (0.32 g., 0.0026 mole, 82%), m.p. and mixture m.p. 127–128°.

Hydrolysis of VIII.—N-[α-(Dibenzylamino)-benzyl]-benzamide (VIII, 1.0 g., 0.00246 mole) was refluxed (eq. 11) with dilute hydrochloric acid (10 ml., 25% by wt.) for 0.25 hr. The mixture was cooled and extracted exhaustively with ether. The aqueous layer was made basic and extracted with ether to give dibenzylamine (88.6%), isolated as N,N-dibenzyl-N'-phenylthiourea (0.73 g., 0.00218 mole), m.p. and mixture m.p. 144–145°, lit.[10] 145–146°.

The ether layer gave benzaldehyde (93%, isolated as its 2,4-dinitrophenylhydrazone, 0.65 g., 0.00226 mole), m.p. 236–237°, and benzamide (0.28 g., 0.00231 mole, 93%), m.p. and mixture m.p. 127–128°.

Acid-Catalyzed Hydrolysis of IX.—A mixture of *p*-chloro-N-[*p*-chloro-α-[(*p*-chlorobenzylidene)-amino]-benzyl]-benzamide (IX, type I, Z = *p*-chloro, 1.0 g., 0.0024 mole) and hydrochloric acid (10 ml., 37% by wt.) was refluxed for 0.25 hr. The reaction product (eq. 3) consisted of *p*-chlorobenzaldehyde (92%, as its 2,4-dinitrophenylhydrazone, 1.44 g., 0.0044 mole, m.p. 266–268°, lit.[11] 267–268°), *p*-chlorobenzamide (0.314 g., 0.00202 mole, 84%, m.p. and mixture m.p. 179–180°), and ammonia.

Reduction of IX with Sodium Borohydride.—Sodium borohydride (0.076 g., 0.002 mole) was added in one portion to a solution of IX (0.836 g., 0.002 mole) in absolute methanol (100 ml.) at 25°. The reaction product (as in eq. 9) was isolated as described previously for VII to give *p*-chloro-N-[*p*-chloro-α-[(*p*-chlorobenzyl)-amino]-benzyl]-benzamide (XVII, 0.58 g., 70%) as a white microcrystalline solid, m.p. 166–168°; mol. wt. calcd. 420, found 409; infrared absorption for NH (3.05 μ) and amide carbonyl (6.05 μ). The product of reduction was the same irrespective of the order of addition of the reagents.

Anal. Calcd. for $C_{21}H_{17}N_2OCl_3$: C, 60.05; H, 4.06; N, 6.67. Found: C, 60.08; H, 4.03; N, 6.53.

Acid-Catalyzed Hydrolysis of N,N'-[Iminobis-(*p*-chlorobenzylidene)]-bis-[*p*-chlorobenzamide] (XVIII).—Hydrolysis of XVIII (type II, Z = *p*-chloro, derived from *p*-chlorobenzylamine, 0.5 g., 0.000873 mole) with refluxing hydrochloric acid (8 ml., 37% by wt.) for 0.25 hr. (as in eq. 4) gave *p*-chlorobenzaldehyde (93%, as its 2,4-dinitrophenylhydrazone, 0.48 g., 0.00163 mole, m.p. 266–268°, lit.[11] m.p. 267–268°), *p*-chlorobenzamide (0.235 g., 0.00151 mole, 86%, m.p. and mixture m.p. 178–179°), and ammonia.

Acid-Catalyzed Hydrolysis of X.—*p*-Nitro-N-[*p*-nitro-α-[(*p*-nitrobenzylidene)-amino]-benzyl]-benzamide (X, type I, Z = *p*-nitro, 1.0 g., 0.00222 mole) is hydrolyzed (0.25 hr.) by refluxing hydrochloric acid (10 ml., 37% by wt.) as in eq. 3 to *p*-nitrobenzaldehyde (90%, as its 2,4-dinitrophenylhydrazone, 1.34 g., 0.00399 mole, m.p. 318–320°, lit.[12] m.p. 320°), *p*-nitrobenzamide (0.33 g., 0.0019 mole, 86%, m.p. and mixture m.p. 201–202°), and ammonia.

Reduction of X with Sodium Borohydride.—Addition of sodium borohydride (0.019 g., 0.0005 mole) to X (0.225 g., 0.0005 mole) in methanol (100 ml.), isolation of the product, and recrystallization from benzene gave *p*-nitro-N-[*p*-nitro-α-[(*p*-nitrobenzyl)-amino]-benzyl]-benzamide (type XIII, 0.108 g., 47%) as a pale yellow microcrystalline solid, m.p. 124–126°; mol. wt. calcd. 451, found 444; infrared absorption for NH (2.9 μ) and amide carbonyl (6.0 μ). An identical product was obtained by addition of X to sodium borohydride.

Anal. Calcd. for $C_{21}H_{17}O_7$: C, 55.87; H, 3.80; N, 15.52. Found: C, 56.05; H, 3.94; N, 15.59.

Acid-Catalyzed Hydrolysis of N,N'-[Iminobis-(*p*-nitrobenzylidene)]-bis-[*p*-nitrobenzamide] (XIX).—Refluxing hydrochloric acid (8 ml., 37% by wt.) converted XIX (type II, Z = *p*-nitro, derived from *p*-nitrobenzylamine, 0.5 g., 0.00081 mole) as in eq. 4 to *p*-nitrobenzaldehyde (94%, as its 2,4-dinitrophenylhydrazone, 0.51 g., 0.00153 mole, m.p. 317–319°, lit.[9] m.p. 320°), *p*-nitrobenzamide (0.23 g., 0.0014 mole, 86%, m.p. and mixture m.p. 201–202°), and ammonia.

Acid-Catalyzed Hydrolysis of XI.—Hydrolysis of N-[*p*-methyl-α-[(*p*-methylbenzylidene)-amino]-benzyl]-*p*-toluamide (XI, type I, Z = *p*-methyl, derived from *p*-methylbenzylamine, 1.0 g., 0.0028 mole) by hydrochloric acid (10 ml., 37% by wt.) as in eq. 3 gave *p*-methylbenzaldehyde (96%, as its 2,4-dinitrophenylhydrazone, 1.65 g., 0.0054 mole, m.p. 232–234°, lit.[12] m.p. 232–234°), *p*-toluamide (0.34 g., 0.00251 mole, 89%, m.p. and mixture m.p. 158–160°), and ammonia.

Reduction of XI with Sodium Borohydride.—Upon addition of sodium borohydride (0.113 g., 0.003 mole) to XI (1.07 g., 0.003 mole) in absolute methanol, hydrolysis of the reaction mixture, and crystallization of the reduction product from benzene, N-[α-[bis-(*p*-methylbenzyl)-amino]-*p*-methylbenzyl]-*p*-toluamide (XX, as in eq. 10) was obtained as white crystals; yield 0.45 g., 65%; m.p. 146–148° (from benzene); mol. wt. calcd. 463, found 454.

Anal. Calcd. for $C_{32}H_{34}N_2O$: C, 83.08; H, 7.41; N, 6.05. Found: C, 83.05; H, 7.37; N, 5.91.

The aqueous filtrate gave *p*-toluamide (eq. 12, 0.167 g., 0.00124 mole, 83%), m.p. and mixture m.p. 157–159°.

Attempts to prepare the normal reduction product (XIII, secondary amine) from XI by reductions at 5 and 25° using ratios of sodium borohydride to substrate of 1:1, 3:2, and 2:1 in absolute methanol were unsuccessful.

Acid-Catalyzed Hydrolysis of N-[*p*-Methyl-α-[(*p*-methylbenzylidene)-amino]-benzyl]-*p*-toluamide (XXII).—Hydrolysis of XXII (0.5 g., 0.00102 mole) with refluxing hydrochloric acid (8 ml., 37% by wt.) for 0.25 hr. gave *p*-methylbenzaldehyde (95%, as its 2,4-dinitrophenylhydrazone, 0.575 g., 0.00191 mole, m.p. 231–233°, lit.[12] m.p. 232–234°), *p*-toluamide (0.243 g., 0.00178 mole, 88%, m.p. and mixture m.p. 158–160°), and ammonia.

Acid-Catalyzed Hydrolysis of XII.—Conversion of N-[*p*-methoxy-α-[(*p*-methoxybenzylidene)-amino]-benzyl]-*p*-anisamide (XII, type I, Z = *p*-methoxy, 1.0 g., 0.00247 mole) was effected by refluxing hydrochloric acid (10 ml., 37% by wt.) in 0.25 hr. as in eq. 3 to *p*-methoxybenzaldehyde (90%, as its 2,4-dinitrophenylhydrazone, 1.38 g., 0.0044 mole, m.p. and mixture m.p. 253–254°), *p*-anisamide (0.318 g., 0.00213 mole, 86%, m.p. and mixture m.p. 165–166°), and ammonia.

Reduction of XII with Sodium Borohydride.—Reduction of XII (1.0 g., 0.00247 mole) in methanol at 25–30° by addition of sodium borohydride (0.095 g., 0.00248 mole) and isolation of the principal product gave N-[α-[bis-(*p*-methoxybenzyl)-amino]-*p*-methoxybenzyl]-*p*-anisamide (XXIII, 0.417 g., 64%) as in eq. 10 as white needles, m.p. 123–124° (from benzene); mol. wt. calcd. 527, found 514; infrared absorption at 3.0 (NH) and 6.12 μ (amide carbonyl).

Anal. Calcd. for $C_{32}H_{34}N_2O_5$: C, 72.98; H, 6.51; N, 5.32. Found: C, 72.76; H, 6.73; N, 5.27.

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