The amines obtained by reducing the oximes of benzoin, diisopropyl ketone, *p*-bromoacetophenone and cyclohexanone were characterized by conversion to their hydrochlorides. α-Phenylethylamine was characterized by conversion to the oxalate.

CHAPEL HILL, NORTH CAROLINA

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[CONTRIBUTION FROM THE COLLEGE OF LIBERAL ARTS AND SCIENCES, TEMPLE UNIVERSITY]

# A New Intramolecular Rearrangement[1]

BY WILLIAM T. CALDWELL AND GEORGE C. SCHWEIKER

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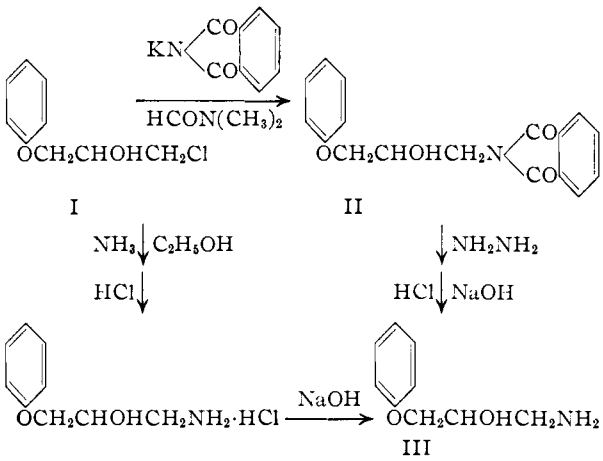
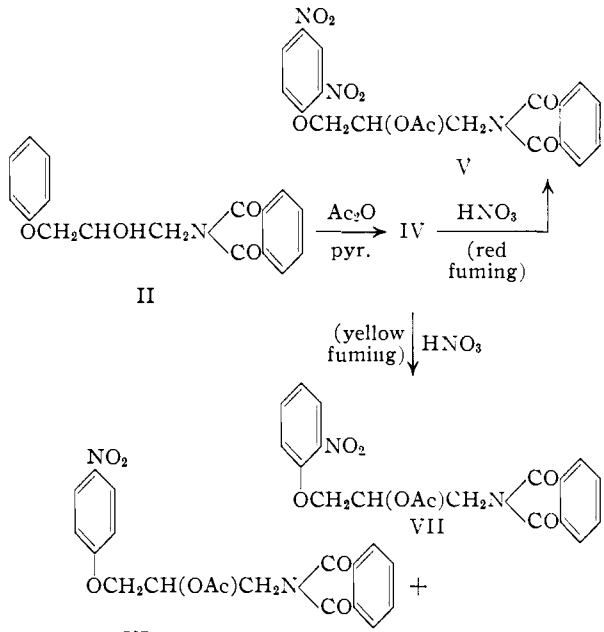
A new example of intramolecular rearrangement is described. It is proved that hydrolysis of 1-(*p*-nitrophenoxy)-2-acetoxy-3-phthalimidopropane (VI) and 1-(*o*-nitrophenoxy)-2-acetoxy-3-phthalimidopropane (VII) gives 1-(*p*-nitroanilino)-2,3-propanediol (VIII) and 1-(*o*-nitroanilino)-2,3-propanediol (IX).

In the final step of an attempted synthesis of 1-(*p*-nitrophenoxy)-2-hydroxy-3-dichloroacetamidopropane (an isomer of Chloramphenicol) it became apparent that the expected intermediate primary amine had not been obtained in spite of excellent analyses in accord with its molecular formula.

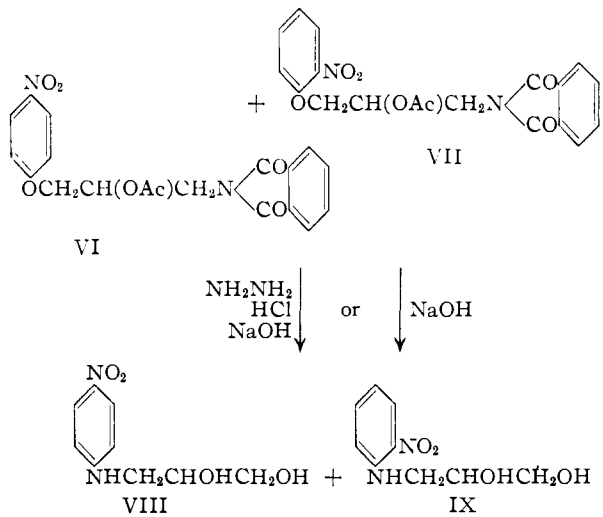
1-Phenoxy-2-hydroxy-3-chloropropane (I) was made as described by Boyd and Knowlton[2] and by Levas and Lefebvre,[3] and treated with potassium phthalimide using dimethylformamide as solvent[4] to prepare 1-phenoxy-2-hydroxy-3-phthalimidopropane (II). 1-Phenoxy-2-hydroxy-3-aminopropane (III) was made from I according to Boyd's directions,[5] and from II by treatment with hydrazine, hydrochloric acid and sodium hydroxide.[4]




All attempts to prepare a crystalline diacetyl derivative of III failed; however, it was found that acetylation of II proved an excellent way of protecting the amino and hydroxyl groups during subsequent nitration. Nitration of 1-phenoxy-2-acetoxy-3-phthalimidopropane (IV) with cold red fuming nitric acid gave 1-(2,4-dinitrophenoxy)-2-acetoxy-3-phthalimidopropane (V), but the action of yellow fuming nitric acid on IV gave a mixture of 1-(*p*-nitrophenoxy)-2-acetoxy-3-phthalimidopropane (VI) and 1-(*o*-nitrophenoxy)-2-acetoxy-3-phthalimidopropane (VII).




When the mixture of VI and VII was hydrolyzed in the manner used to hydrolyze II, only a 5% yield of a mixture of 1-(*p*-nitroanilino)-2,3-propanediol (VIII) and 1-(*o*-nitroanilino)-2,3-propanediol (IX) was obtained. It was surprising to find, however, that the mixture of VI and VII gave good




(1) Taken from a thesis submitted by George C. Schweiker in partial fulfillment of the requirements for the degree of Master of Arts.

(2) D. Boyd and H. Knowlton, *J. Chem. Soc.*, **95**, 1802 (1909).

(3) E. Levas and H. Lefebvre, *Compt. rend.*, **222**, 555 (1946).

(4) J. Sheehan and W. Bolhofer, THIS JOURNAL, **72**, 2786 (1950).

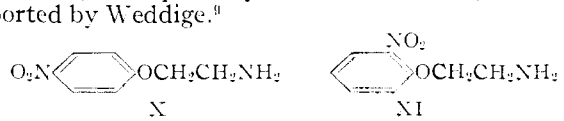
(5) D. Boyd, *J. Chem. Soc.*, **97**, 1791 (1910).

yields of a mixture of VIII and IX upon hydrolysis with relatively dilute sodium hydroxide solution.

VIII was obtained in pure form by extraction of the ortho and para mixture; IX was obtained pure by chromatographic adsorption. Various tests and reactions showed that hydrolysis of VI and VII had not produced the expected 1-(*p*-nitrophenoxy)-2-hydroxy-3-aminopropane and 1-(*o*-nitrophenoxy)-2-hydroxy-3-aminopropane. In particular, failure of methyl dichloroacetate to bring about dichloroacetylation forced us to consider the possibility of an intramolecular rearrangement to a compound no longer containing a free primary amino group. This possibility became a probability when a search of the literature revealed that the m.p. of IX was close to that of 1-(*o*-nitroanilino)-2,3-propanediol reported by Karrer, Saloman, Schöpp and Schlitter.[6] VIII and IX were made accordingly by the method of Karrer, *et al.*, and the compounds prepared in these different ways were compared. Mixed m.p. determinations, infrared absorption spectra and X-ray diffraction patterns, as well as melting points, solubilities and colors showed that the compounds prepared by these different procedures were identical.

This rearrangement is a new example of intramolecular nucleophilic displacements, many of which are known collectively as the Smiles rearrangement[7]; it appears to be the first recognition of a case of an amino group on an alkyl side chain displacing the alkoxy group from an aromatic nucleus activated for nucleophilic attack by the presence of a nitro group. Evans and Smiles,[7] and Bunnett and Zahler,[8] have summarized the several sorts of Smiles rearrangements which have been observed in the following way where in X-C-C-YH the group YH is separated from X by two intervening carbon atoms. In previously described rearrangements, YH has stood for NHacyl, etc., and X for $SO_2$, S, O, etc.[8] In the present rearrangement, YH is $NH_2$(alkyl) and X is O and the intervening chain contains three atoms of carbon.

In the light of this rearrangement, it is logical to assume that rearrangements of other nitrophenoxy alkyl amines may have escaped detection. For example, this would seem to be true of the compounds 1-(*p*-nitrophenoxy)-2-aminoethane (X) and 1-(*o*-nitrophenoxy)-2-aminoethane (XI) reported by Weddige.[9]



In the preparation of X and XI, Weddige heated the corresponding nitrophenoxy-β-bromoethanes with alcoholic ammonia at 100–120° for several hours. The vermilion ortho compound (m.p. 72–73°) and its yellow para isomer (m.p. 108–109°) resemble in color and m.p. the compounds *p*-nitroanilinoethanol (m.p. 110–110.5°) and *o*-nitroanilinoethanol (m.p. 76–76.5°) prepared by Kremer[10] and various others by heating aminoethanol in the presence of anhydrous sodium carbonate with the respective chloronitrobenzenes.

Weddige apparently could not isolate the hydrochloride of either X or XI and he stated that the presumed hydrochloride of XI in a concentrated hydrochloric acid solution was decomposed by the addition of water. Furthermore, when he warmed XI with a mole of benzoyl chloride two substances were formed; one compound was a monobenzoyl derivative, and the other was a dibenzoyl derivative which in Weddige's opinion was the N,N-dibenzoyl derivative of XI. It does not seem likely that XI would form a N,N-dibenzoyl derivative under these conditions; on the other hand, if XI had rearranged, in a fashion analogous to the rearrangement proved in this paper, to form *o*-nitroanilinoethanol, it is easy to understand how a monobenzoyl derivative and a N,O-dibenzoyl derivative could be formed. Also, if X and XI had rearranged to form the corresponding nitroanilino compounds the instability of the hydrochloride salts would then be explained.

We wish to thank Eli Lilly and Company for data on infrared absorption and X-ray diffraction, and the Temple University Committee on Research and Publications for a Grant-in-Aid.

## Experimental[11]

**1-Phenoxy-2-hydroxy-3-phthalimidopropane** (II).—Sheehan and Bolhofer[4] reported that dimethylformamide is an excellent solvent for the Gabriel reaction. Accordingly, II was made from 1-phenoxy-2-hydroxy-3-chloropropane[2,3] and potassium phthalimide using dimethylformamide in a manner analogous to that described by Sheehan and Bolhofer. Powdery white II was obtained in 76% yield, m.p. 108–110°.

*Anal.* Calcd. for $C_{17}H_{15}O_4N$: C, 68.67; H, 5.09; N, 4.71. Found: C, 68.77; H, 5.15; N, 4.98.

**1-Phenoxy-2-hydroxy-3-aminopropane** (III) was prepared by hydrolyzing II in a manner similar to that used by Sheehan and Bolhofer[4] to hydrolyze various other phthalimido compounds; also, III was prepared from 1-phenoxy-2-hydroxy-3-chloropropane[2,3] as described by Boyd,[5] which required the isolation of the stable hydrochloride of III. A mixed m.p. of the compounds prepared in these two different ways resulted in no depression; m.p. 96–97°.

**1-Phenoxy-2-acetoxy-3-phthalimidopropane** (IV).—The acetyl derivative of II was prepared in the usual manner using acetic anhydride and anhydrous pyridine. White, crystalline IV was recovered in 92.5% yield, m.p. 85–87°.

*Anal.* Calcd. for $C_{19}H_{17}O_5N$: N, 4.13. Found: N, 4.30.

**1-(2,4-Dinitrophenoxy)-2-acetoxy-3-phthalimidopropane** (V) resulted from the addition of IV to red fuming nitric acid (sp. gr. 1.6) kept at a temperature of −3 to 3°. After 10 minutes at this temperature the solution was poured into ice-water and the product filtered off and washed with 5% sodium bicarbonate and water. Recrystallizations from alcohol, chloroform, ethyl acetate–chloroform and benzene gave a 23.7% yield of pale yellow crystalline V, m.p. 194–196°.

*Anal.* Calcd. for $C_{19}H_{15}O_9N_3$: N, 9.79. Found: N, 9.74.

**Nitration of IV using yellow fuming nitric acid** gave a mixture of 1-(*p*-nitrophenoxy)-2-acetoxy-3-phthalimidopropane

(6) P. Karrer, H. Saloman, K. Schöpp and E. Schlitter, *Helv. Chim. Acta*, **17**, 1165 (1934).

(7) W. Evans and S. Smiles, *J. Chem. Soc.*, 181 (1935).

(8) J. Bunnett and R. Zahler, *Chem. Revs.*, **59**, 273 (1951).

(9) A. Weddige, *J. prakt. Chem.*, [2] **24**, 241 (1881).

(10) C. Kremer, THIS JOURNAL, **61**, 1321 (1939).

(11) All melting points are uncorrected. Elemental analyses were performed by the Clark Microanalytical Laboratory, Urbana, Illinois.

(VI) and 1-(*o*-nitrophenoxy)-2-acetoxy-3-phthalimidopropane (VII). A solution of yellow fuming nitric acid (sp. gr. 1.5) in glacial acetic acid was added to a solution of IV in 4 parts of glacial acetic acid to 1 part of acetic anhydride at 80°, and the resulting red solution was kept at 80° for another hour before it was poured into ice-water. Filtration and washing with 5% sodium bicarbonate and water, followed by trituration with boiling ethanol produced a crystalline mixture of VI and VII which was recrystallized from benzene. The pale yellow mixture was obtained in 81.6% yield, m.p. 140–146°.

Separation of the ortho and para isomers at this stage seemed inadvisable because of the great loss of material during recrystallizations of an analytical sample. The results of a nitrogen analysis on this sample, m.p. 158–160°, were in keeping with the composition of either VI or VII or a mixture of the two.

*Anal.* Calcd. for $C_{19}H_{16}O_7N_2$: N, 7.29. Found: N, 7.48.

1-(*p*-**Nitroanilino**)-**2,3-propanediol** (**VIII**). **A.**—The mixture of VI and VII (m.p. 140–146°) was hydrolyzed in the manner[4] used to hydrolyze II, except that the refluxing time with hydrazine (2 moles in this case) was lengthened to 6 hours, and refluxing with 1 to 1 hydrochloric acid was lengthened to 8 hours. The dark oil so produced yielded only 5.4% of orange-yellow crystalline material, m.p. 112–114°, after many extractions and fractional crystallizations with various solvents.

*Anal.* Calcd. for $C_9H_{12}O_4N_2$: C, 50.94; H, 5.70; N, 13.20. Found: C, 50.74; H, 5.70; N, 13.15.

It was found later that this constant melting material was still a mixture of the ortho and para isomers.

**B.**—Sixty grams (0.156 mole) of the mixture of VI and VII (m.p. 140–146°) was mixed with 20 g. of sodium hydroxide (0.50 mole) in 160 ml. of water and refluxed for 1 hour. As reflux temperature was approached, the two phase system changed into a deep red solution after approximately 5 minutes of heating. After cooling, orange crystals were filtered off and recrystallized from water and ethyl acetate. (Acidification of the filtrate produced phthalic acid.) The product was extracted with three small portions of chloroform, and the material which did not dissolve was extracted with an alcohol–chloroform mixture. The yellow crystals (VIII) still remaining undissolved were recrystallized from alcohol–acetone and alcohol–chloroform; m.p. 126–127°. From many fractional crystallizations of the chloroform extracts, two separate piles of material were collected and recrystallized separately from ethyl acetate. The yield of yellow VIII was 2 g., m.p. 126–127°; the yield of the orange-yellow mixture of VIII and its ortho isomer (IX) was 18 g., m.p. 106–112°.

**C.**—VIII was made in 6% yield, m.p. 126–127°, in a fashion analogous to that described by Karrer,[6] *et al.*, for the preparation of its ortho isomer (IX), using 1-amino-2,3-propanediol[12] and *p*-nitrochlorobenzene.

*Anal.* Calcd. for $C_9H_{12}O_4N_2$: N, 13.20. Found: N, 13.06.

A mixed m.p. determination of VIII prepared as described in B and C gave no depression.

1-(*o*-**Nitroanilino**)-**2,3-propanediol** (**IX**). **A.**—Recrystallizations of the mixture of VIII and IX, as prepared in B above (m.p. 106–112°), from chloroform gave a constant melting mixture, m.p. 112–114°, and the yield decreased to 4 g. However, orange-yellow IX, m.p. 117–118°, was isolated from this constant melting mixture by chromatographic adsorption. The mixture was deposited upon alumina from chloroform solutions, developed with 10% absolute ethanol in chloroform, and eluted with methanol.

B.—IX was made in 14% yield as described by Karrer,[6] *et al.*, m.p. 117–118°.

A mixed m.p. determination of IX prepared as described in A and B gave no depression.

**1-(*o*-Nitroanilino)-2,3-propanediol hydrochloride** could not be isolated from an aqueous hydrochloric acid solution of IX by evaporation of the solvent in a vacuum desiccator. However, the white salt was obtained by passing hydrogen chloride gas through an ether solution of IX, containing a small amount of methanol. The salt turned pale yellow during filtering and washing with ether, and a portion in moist air very quickly decomposed into the original orange-yellow IX.

(12) L. and E. Knorr, *Chem. Ber.*, **32**, 750 (1899).

PHILADELPHIA 22, PENNA.

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[CONTRIBUTION FROM THE METCALF CHEMICAL LABORATORIES, BROWN UNIVERSITY]

# 2-Propyl-4-ethyl-3-nitrosoöxazolidine, a Novel Product from the Nitrous Acid Deamination of 2-Amino-1-butanol

BY HAROLD R. NACE AND MORTON H. GOLLIS[1]

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The nitrous acid deamination of 2-amino-1-butanol in acetic acid yields 2-propyl-4-ethyl-3-nitrosoöxazolidine (49–52%), 1,2-butanediol (4%) and crotyl alcohol (4%). When the reaction is carried out in hydrochloric acid, 2-chloro-1-butanol (2%) is also obtained. The nitrosoöxazolidine is cleaved by acid to *n*-butyraldehyde and the starting amino alcohol. The nitrosoöxazolidine was synthesized by nitrosation of the oxazolidine, formed by the condensation of *n*-butyraldehyde with 2-amino-1-butanol.

Many examples of the reaction of β-amino alcohols with nitrous acid have been reported.[2] In the majority of the cases studied products with rearranged carbon skeletons have resulted, the products being analogous to those of the pinacol rearrangement. However, the reaction has been complicated by one or more factors: (a) The presence of one or more aryl groups on the substituent-bearing carbon atoms has superimposed migratory aptitude and steric effects on the course of the rearrangement.[3] (b) The substituents were attached to carbon atoms incorporated in alicyclic structures, thus bringing into play the effect of polar and equatorial bonds on the ease and direction of the rearrangement.[4] Simple aliphatic amino alcohols would be free of these complicating factors, and a study of them should facilitate the understanding of the more involved cases.

A search of the literature revealed only a few examples of the reaction of simple aliphatic amino alcohols with nitrous acid. Krassusky and Duda[5] obtained in unstated yields pinacol and pinacolone from the reaction of 2,3-dimethyl-3-amino-2-butanol with nitrous acid. Neuberg and Rewald[6]

(1) Research Corporation Fellow, 1951–1952.

(2) G. W. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, Chap. 12.

(3) For further discussion and references see P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950).

(4) G. E. McCasland, *ibid.*, **73**, 2293 (1951).

(5) K. Krassusky and L. Duda, *J. prakt. Chem.*, [2] **77**, 96 (1908).

(6) C. Neuberg and B. Rewald, *Biochem. Z.*, **67**, 132 (1914).