# The Deamination of *erythro-* and *threo-*1,2-Diphenyl-2-aminoethanol[1]

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The nitrous acid catalyzed deaminations of *erythro-* and *threo-*1,2-diphenyl-2-aminoethanol have been reinvestigated. The deamination product of the *erythro* isomer contains 15% *trans*-stilbene oxide, 9% desoxybenzoin, 44% diphenylacetaldehyde, 12% *meso*-hydrobenzoin, and 20% *dl*-hydrobenzoin. The *threo* amino alcohol gives 69% diphenylacetaldehyde, 8% *meso*-hydrobenzoin, and 23% *dl*-hydrobenzoin. When the D-(−)-*erythro* compound was subjected to deamination, D-(+)-hydrobenzoin and stilbene oxide were obtained, while the L-*threo* amino alcohol gave L-(−)-hydrobenzoin. These mechanistic implications of these results are discussed. During the course of this work, it was observed that diphenylacetaldehyde undergoes a base-catalyzed autoxidation to benzophenone and formic acid. A mechanism for this reaction is presented.

Although various workers have studied the course of the deamination of diaryl-2-amino alkanols in considerable detail,[3] the deamination products of the structurally simple compounds, *erythro-* and *threo-*1,2-diphenyl-2-aminoethanol, have not been fully characterized, although several studies of their deamination have been carried out. The first reported study of this reaction was by Erlenmeyer,[4] who obtained both *meso-* and *dl*-hydrobenzoin, along with an oil which appeared to contain some diphenylacetaldehyde. In the years just prior to 1930 this work was repeated by Read[5] who also obtained the hydrobenzoins, along with an oil which apparently contained some benzophenone. The hydrobenzoins were also obtained from this reaction by Felkin, but again the bulk of the reaction product remained unidentified.[6]

The *dl-erythro-*1,2-diphenyl-2-aminoethanol used in this study was prepared by the hydrogenation of benzoin oxime,[7] and the *threo* isomer was prepared by isomerization of the *erythro* compound.[7] The deaminations were carried out in dilute acetic acid at 0°, and the products were subjected to qualitative analysis by thin layer chromatography and infrared spectroscopy. The relative amounts of the various products were determined by chromatography on neutral alumina.[8] The over-all yield of deamination products ranged from 63 to 87%, and the results obtained from both isomers are summarized in Table I.

Collins and co-workers have explained the distribution of products obtained from the deamination of 1,1-diaryl-2-amino alcohols in terms of the ground-state conformation of the amino alcohols.[3a-d] In order to obtain some insight into the amount of each of the principal contributing conformational isomers of the amino alcohols, the n.m.r. spectrum of each amino alcohol was determined in dilute acid, and the amount of the various conformers was calculated.[9] From the n.m.r. data it was calculated that conformer I accounted for 20 ± 10% of the ground-state population of the

### TABLE I

| Products | Mole % from *threo* isomer[a] | Mole % from *erythro* isomer[a] |
|---|---|---|
| *trans*-Stilbene oxide | Trace[b] | 15 |
| Desoxybenzoin | Trace[b] | 9 |
| Diphenylacetaldehyde | 69[c] | 44[c] |
| *meso*-Hydrobenzoin | 8 | 12 |
| *dl*-Hydrobenzoin | 23 | 20 |

[a] Average of five runs, maximum deviation, ±5%. [b] Detected by thin layer chromatography only, could not be isolated. [c] Isolated as benzophenone (see text).
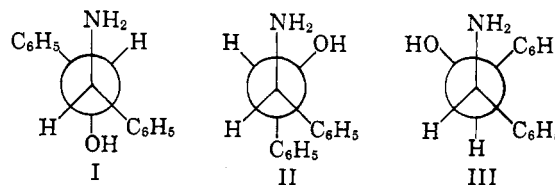


I　　　　II　　　　III

*erythro* isomer, with the remaining 80 ± 10% divided between conformers II and III.

In the *threo* isomer, the n.m.r. data indicated that conformer IV was present to the extent of 80 ± 10%, with the balance being divided between V and VI. It may be assumed that, since VI both lacks hydrogen



IV　　　　V　　　　VI
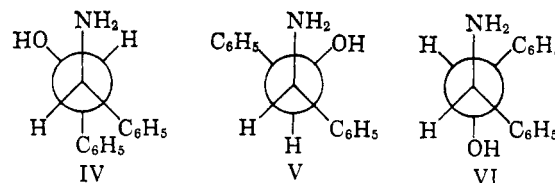
bonding between the amino and hydroxyl groups and has all the bulky groups in a gauche relationship, it should be present to a very small extent, and that virtually all the remaining *threo* isomer exists as conformer V.

Deamination of the *threo* amino alcohol would then give rise to carbonium ions VII and VIII, to the extent of 80 and 20%, respectively. It would be expected that ion VII would give rise to the 69% diphenylacetaldehyde *via* phenyl migration, and the remaining

(1) Presented at the XIXth International Congress of Pure and Applied Chemistry, London, July 1963.

(2) (a) Taken from the thesis submitted by R. P. Elliott in partial fulfillment of the requirements for the Ph.D. degree, May 1964. (b) National Defense Education Act Fellow, 1960–1963.

(3) (a) C. J. Collins, M. M. Staum, and B. M. Benjamin, *J. Org. Chem.*, **27**, 3525 (1962); (b) B. M. Benjamin and C. J. Collins, *J. Am. Chem. Soc.*, **83**, 3662 (1961); (c) B. M. Benjamin, P. Wilder, and C. J. Collins, *ibid.*, **83**, 3654 (1961); (d) B. M. Benjamin, H. J. Schaeffer, and C. J. Collins, *ibid.*, **79**, 6160 (1957); (e) P. I. Pollak and D. Y. Curtin, *ibid.*, **73**, 992 (1951); (f) P. I. Pollak and D. Y. Curtin, *ibid.*, **72**, 961 (1950).

(4) E. Erleymeyer, *Ann.*, **307**, 113 (1899).

(5) (a) J. Read and I. G. M. Campbell, *J. Chem. Soc.*, 2377 (1930); (b) J. Read, J. Campbell, and T. Barker, *ibid.*, 2305 (1929); (c) J. Read and C. C. Steele, *ibid.*, 910 (1927).

(6) H. Felkin, *Bull. soc. chim. France*, 20 (1959).

(7) J. Weijlard, K. Pfister, E. F. Swanzey, C. A. Robinson, and M. Tschler, *J. Am. Chem. Soc.*, **73**, 1216 (1951).

(8) An attempt was made to employ silica gel as an adsorbent for the separation of these compounds; however, it was found that *trans*-stilbene oxide was converted to diphenylacetaldehyde under these conditions.

(9) B. M. Benjamin, private communication. The aliphatic protons of the *erythro* isomer have J = 4.8 c.p.s., those of the *threo* 10 c.p.s. We would like to thank Dr. Benjamin for carrying out these measurements and the accompanying calculations. A detailed description of this work will be included in Dr. Benjamin's forthcoming publication.

HO   H                    C₆H₅   OH
H—(+)—C₆H₅           H—(+)—C₆H₅
   C₆H₅                        H
    VII                       VIII
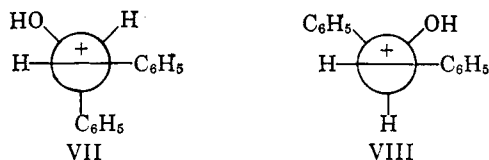
11% of ion VII would react with solvent to give *dl*-hydrobenzoin. Although in principle ion VII could give rise to *meso*-hydrobenzoin, it has been shown that in reactions of unbridged carbonium ions attack of hydroxyl in such a manner as to eclipse a phenyl group is not a principal reaction path when alternative routes are available.[10] The 8% *meso*-hydrobenzoin, remaining 12% *dl*-hydrobenzoin, and trace of desoxybenzoin would be derived from ion VIII.

Although it has recently been shown that in the deamination of 1,2,2-triphenylethylamine the rate of rotation of the carbonium ion, phenyl migration, and nucleophilic attack all occur at about the same rate,[11] rotation of ions VII and VIII must necessarily be slow compared to various reactions of these ions, since the products obtained from the deamination of the 1,2-diphenylaminoethanols are not consistent with those expected from rotation of the various ions. For instance, rotation of ion VII would give rise to ions IXa and IXb which should afford appreciable quanti-

OH              H              OH
H—(+)—C₆H₅   H—(+)—C₆H₅   H—(+)—C₆H₅
C₆H₅   H      HO   C₆H₅      C₆H₅   H
    IXa           IXb            X
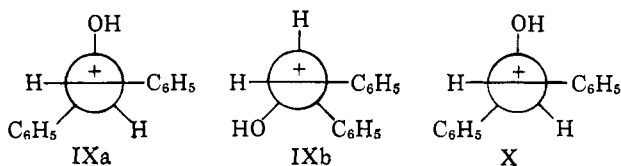
ties of *trans*-stilbene oxide and desoxybenzoin, respectively, neither of which are found in more than trace amounts in the reaction mixture. Rotation of ion VIII would give rise to ion X which would also be expected to give *trans*-stilbene oxide.[12]

The interpretation of the deamination of the *erythro* amino alcohol is complicated by the presence of all three possible conformers (I to III). First, in the deamination of the *threo* compound the ratio of frontside to backside attack of hydroxyl on ions VII and VIII is 2.9 (ratio of *dl*- to *meso*-hydrobenzoin), while in the deamination of the *erythro* compound the ratio of frontside to backside attack (ratio of *meso*- to *dl*-hydrobenzoin) is 0.6. Based on the ground-state conformation of *erythro*-1,2-diphenyl-2-aminoethanol the expected carbonium ions formed in the deamination should be XI, XII, and XIII (from I, II and III, respectively); however a consideration of the various carbonium ions obtained on rotation of ions XI through XIII indicates that rotation of these species cannot be excluded.
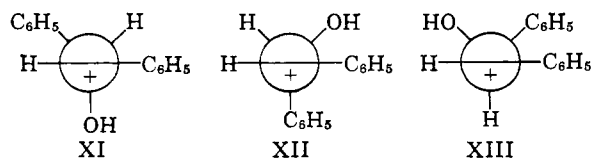
C₆H₅   H      H   OH      HO   C₆H₅
H—(+)—C₆H₅   H—(+)—C₆H₅   H—(+)—C₆H₅
   OH            C₆H₅           H
    XI            XII            XIII

The bulk of the *trans*-stilbene oxide is probably obtained from ion XI (or perhaps from a concerted intramolecular displacement of nitrogen from the diazonium salt) *via* a protonated stilbene oxide XIV. XIV can also give rise to *dl*-hydrobenzoin through an inter-

H⁺                      H δ⁺
O                       O
H—⧹C₆H₅              H—⧹ δ⁺ C₆H₅
C₆H₅   H                C₆H₅   H
    XIV                    XV

mediate such as XV, similar to that suggested for the acid-catalyzed *cis* opening of stilbene epoxides,[13] thus perhaps accounting for the small ratio of frontside to backside attack observed for the *erythro* isomer.

Ion XII would be expected to give rise to diphenylacetaldehyde and *meso*-hydrobenzoin, while ion XIII should afford desoxybenzoin and both hydrobenzoins. None of the products arise from a direct acid-catalyzed reaction of stilbene oxide, since stilbene oxide and also the hydrobenzoins are stable to the reaction conditions.

When the optically active amino alcohols were treated with nitrous acid, the D-*erythro* compound afforded D-(+)-hydrobenzoin and D-*trans*-stilbene oxide, while the L-*threo* amino alcohol gave L-(−)-hydrobenzoin. Since the absolute configurations of all the compounds involved are known,[7,14] it follows from the above that the optically active products are formed from the *erythro* amino alcohol with inversion at the site of the amino group, while the *threo* compound affords the optically active glycol with net retention of configuration. This is consistent with the mechanistic paths shown, and the results are in agreement with those obtained by Read and Steele.[5c]

In the course of carrying out the separation of the various components of these reaction mixtures by chromatography on alumina, considerable quantities of benzophenone were obtained. Since there had been no indication that benzophenone was present in the crude reaction mixtures (no carbonyl absorption above 6 μ), it was apparent that benzophenone was an artifact, obtained during the course of chromatography. Also, although the crude reaction mixtures showed carbonyl absorption at 5.78 μ, attributable to diphenylacetaldehyde, none of this material could be obtained following chromatography on alumina. It was found, however, that when the crude reaction product was chromatographed on silica gel 61% of the material isolated was diphenylacetaldehyde.[8] In addition, when a pure sample of this aldehyde was allowed to stand at room temperature for a few weeks, partial conversion to benzophenone occurred.[15] When a stream of oxygen was bubbled through a solution of diphenylacetaldehyde in ethanol for 16 hr., only slight conversion to benzophenone was observed; however, when the same reaction was carried out in the presence of sodium

(10) C. J. Collins, W. A. Bonner, and C. T. Lester, *J. Am. Chem. Soc.*, **81**, 466 (1959).

(11) C. J. Collins and B. M. Benjamin, *ibid.*, **85**, 2519 (1963).

(12) In discussing the rotation of these ions we have only considered those rotations where phenyl or hydroxyl will eclipse a hydrogen during rotation.

(13) The *cis* opening of stilbene oxides is well documented and has been discussed in detail by both J. H. Brewster [*J. Am. Chem. Soc.*, **78**, 4061 (1956)] and H. Wasserman and N. Aubrey [*ibid.*, **78**, 1726 (1956)].

(14) (a) G. Lyle and W. Lacroix [*J. Org. Chem.*, **28**, 900 (1963)] have recently corrected the assignment of configuration for the *threo* amino alcohol. (b) G. Berti and F. Bottari [*ibid.*, **25**, 1286 (1960)] have discussed in detail the absolute stereochemistry of the hydrobenzoins and *trans*-stilbene oxide.

(15) A preliminary communication concerning this work appeared in *Chem. Ind.* (London), 650 (1963).

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acetate, much benzophenone was formed; and, after acidification and heating, ethyl formate was also detected as a reaction product.

On the basis of these data it is apparent that diphenylacetaldehyde undergoes base-catalyzed air oxidation to benzophenone. A mechanism which accounts for the observed facts is presented in Chart I.

This also accounts for the observation that benzophenone was obtained by earlier workers from the deamination of the diphenylaminoethanols,[4,5] and also from other reactions where diphenylacetaldehyde was an expected product.[14]

## Experimental[16]

erythro- and threo-1,2-Diphenyl-2-aminoethanol.—The erythro isomer was prepared from benzoin oxime using essentially the procedure of the Merck group[7]; however, contrary to the results reported by these workers, better yields of amino alcohol (75–80%) were obtained when the hydrogenation was carried out in neutral solution, rather than in an acidic medium. When the reduction was carried out in acid, a 55% yield of the desired product, along with a considerable quantity of meso-hydrobenzoin was obtained. Resolution of this compound via the L-(+)-glutamic acid salt[7] gave the optically active amino alcohol, $[\alpha]^{22}$D −8.0° (c 0.60, ethanol), lit.[7] $[\alpha]^{22}$D −10.1° (c 0.59, ethanol). Both racemic and optically active erythro-1,2-diphenyl-2-aminoethanol were converted to the threo isomer by the published procedure.[7] The optically active threo compound had $[\alpha]^{22}$D −122° (c 0.60, ethanol), lit.[7] $[\alpha]^{22}$D −124°.

Deaminations.—In a typical experiment, a solution of 2.0 g. of erythro-1,2-diphenyl-2-aminoethanol in 40 ml. of water and 20 ml. of acetic acid was cooled to 0°, and a chilled solution of 2.0

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(16) Melting points were determined on a Hershberg melting point apparatus and are corrected. Infrared spectra were carried out as liquid films or as potassium bromide pellets using a Perkin-Elmer Model 137 spectrophotometer. Rotations were determined using a Rudolph Model 70 polarimeter.

g. of sodium nitrite in 24 ml. of water was added dropwise. The reaction mixture was stirred at 0° for 2.5 hr., diluted with water, and extracted with ether. The ethereal solution was washed successively with water, saturated sodium bicarbonate, and two more portions of water, and dried; the solvent was removed at reduced pressure to give 1.60 g. of crude product.

The crude reaction product was dissolved in a measured quantity of benzene, diluted with four times that volume of hexane, and chromatographed on 100 g. of neutral (Bio-Rad) alumina. Elution with successively 4:1 hexane–benzene, 7:3 hexane–benzene, 1:1 hexane–benzene, 1:1 benzene–ether, ether, 3, 5, and 10% isopropyl alcohol in ether, 10% methanol in ether, and finally a mixture of 15:4:1 ether–methanol–water gave 0.180 g. of trans-stilbene oxide, 0.139 g. of desoxybenzoin, 0.655 g. of a mixture of diphenylacetaldehyde and benzophenone, 0.180 g. of meso-hydrobenzoin, and 0.315 g. of dl-hydrobenzoin. Each fraction eluted from the column was checked for homogeneity by thin layer chromatography on alumina G, and characterized by infrared spectroscopy and/or isolation and comparison with authentic samples.

When the optically active erythro amino alcohol was treated under these conditions, there was obtained optically active trans-stilbene oxide, $[\alpha]^{22}$D +344° (c 0.500, benzene), lit.[14b] $[\alpha]$D +365° (c 0.500, benzene), and D-(+)-hydrobenzoin, $[\alpha]^{22}$D +95° (c 1.000, ethanol), lit.[14b] $[\alpha]$D +93.5° (c 0.998, ethanol).

The figures reported in Table I are the averages of the run described above and four others carried out in a similar manner.

Treatment of 1.0 g. of threo amino alcohol under the above conditions gave 0.333 g. of the mixture of diphenylacetaldehyde and benzophenone, 0.066 g. of meso-hydrobenzoin, and 0.128 g. of dl-hydrobenzoin. The optically active threo compound gave L-(−)-hydrobenzoin, $[\alpha]^{22}$D −95° (c 1.000, ethanol), lit.[14b] $[\alpha]$D −93.5° (c 0.998, ethanol). The figures in Table I are also the averages for five runs.

When trans-stilbene oxide and meso- and dl-hydrobenzoin were each stirred in aqueous acetic acid under the reaction conditions described above, thin layer chromatography of the crude reaction products indicated that the starting materials were recovered unchanged.

Air Oxidation of Diphenylacetaldehyde.—To a solution of 1.0 g. of diphenylacetaldehyde in 50 ml. of ethanol was added 0.05 g. of sodium acetate. Air was bubbled through the solution for 16 hr.; the reaction mixture was concentrated to a small volume, diluted with water, and extracted with ether. The etheral extract was washed with water and dried; the solvent was removed in vacuo to give 0.91 g. of a viscous oil, the infrared spectrum of which indicated that it was essentially pure benzophenone. When the reaction was carried out under the same conditions, but in the absence of sodium acetate, the crude product consisted almost entirely of recovered diphenylacetaldehyde.

In order to detect the presence of formic acid in the reaction product, the air oxidation was carried out using 0.05 g. of sodium hydroxide in place of the sodium acetate. After passing air through the reaction mixture for 16 hr., sufficient concentrated hydrochloric acid to make the solution acidic was added, it was heated under reflux 3 hr., and the solvent was distilled off slowly. Gas chromatography of the first several milliliters of distillate indicated the presence of ethyl formate.