# Mechanism of the Conversion of Phenylglyoxal to Mandelic Acid

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Three reasonable mechanisms may be considered for the base-catalyzed conversion of phenylglyoxal (I) to mandelic acid. Mechanism A,[1] an intramolecular version of one of the attractive mechanisms of the Cannizzaro reaction,[2] involves the intramolecular migration of a hydrogen atom in the intermediate anion II. Mechanism B,[1]
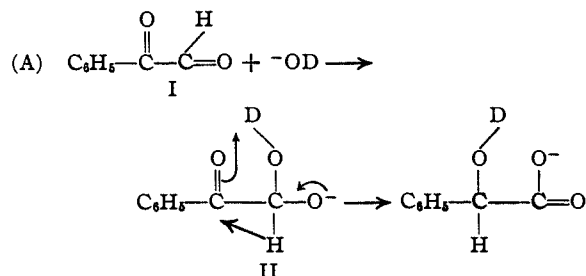
similar to that of the benzil–benzilic acid conversion,[3] involves migration of the phenyl group in III, an intermediate
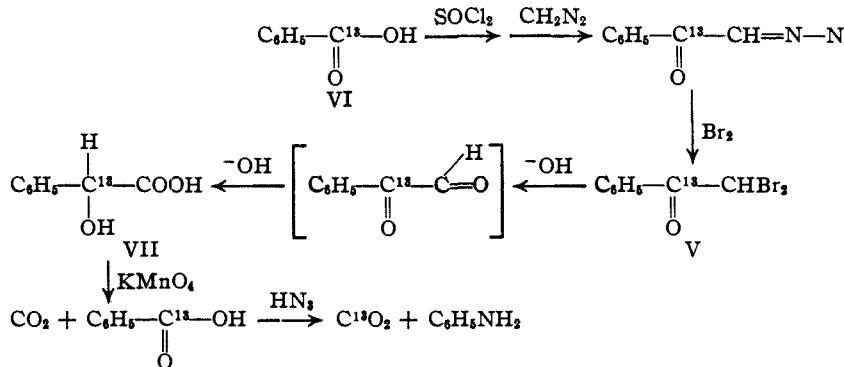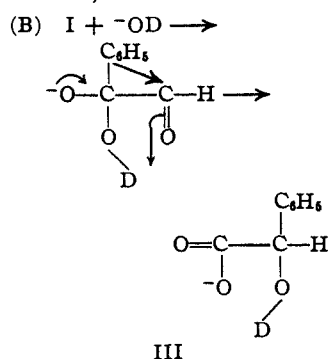
closely related to II. Finally, in mechanism C direct removal of a proton from I establishes equilibrium with the tautomeric hydroxy-ketene IV which adds water forming mandelic acid.
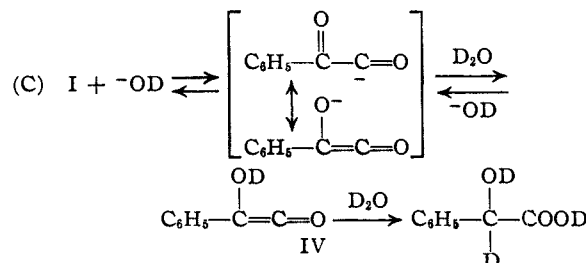
however, impossible to distinguish between mechanisms A, B and C on a kinetic basis alone.
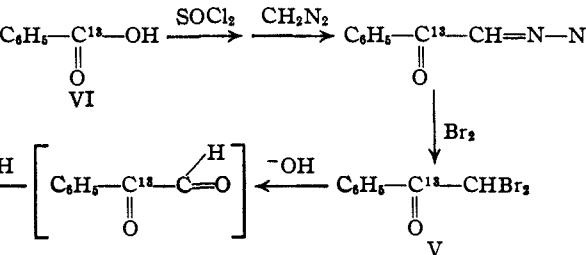
Alexander, finding that the rate of the phenylglyoxal–mandelic acid reaction follows second-order kinetics, has supported mechanism A. It is,

Fredenhagen and Bonhoeffer[4] have invalidated mechanism C for the conversion of glyoxal to glycolic acid only by showing that solvent deuterium does not intervene in this reaction. They have not extended their experiments to I or any other monosubstituted glyoxal.

The following experiments afford evidence that there is no rearrangement of the carbon skeleton in the phenylglyoxal–mandelic acid transformation, mechanism B thereby being excluded. ω,ω-Dibromoacetophenone (V), prepared in two steps from benzoic acid containing 2.32% C^{13} in the carboxyl group (VI), is hydrolyzed with potassium hydroxide.[5] Oxidation of the resulting mandelic acid (VII) with permanganate has given carbon dioxide of normal C^{13} content and benzoic acid from which carbon dioxide containing 2.24% C^{13} has been obtained by the Schmidt reaction.[6,6a]

Extension of Bonhoeffer's work[4] to phenylglyoxal has invalidated mechanism C for a monosub-

stituted glyoxal. When I is treated with barium oxide in deuterium oxide there is obtained mandelic acid which, after equilibration with excess 0.5 N barium hydroxide,[7] contains no deuterium.

Only mechanism A is consistent with the available facts: no rearrangement of the carbon skeleton; the intramolecular transfer of hydrogen; the facile reaction of mesitylglyoxal[8]; and the

(4) Fredenhagen and Bonhoeffer, Z. physik. Chem., A181, 379 (1938).

(5) Ayres and Hauser[1] have isolated I as an intermediate in this reaction.

(6) Oesterlin, Z. angew. Chem., 45, 536 (1932).

(6a) Added in proof: O. Kenton Neville and Weldon G. Brown, [American Chemical Society, New York Meeting, September 18, 1947] have excluded mechanism B by a series of reactions differing significantly from ours.

(7) Two experiments prove that deuterium is not removable from the α-carbon of mandelic acid during the equilibration: the one in which α-hydroxyphenylacetic-d acid loses no deuterium in aqueous baryta at room temperature; the other, by McKenzie and Wren [J. Chem. Soc., 115, 603 (1918)], in which (−)-mandelic acid is racemized only 2.2% on treatment with 0.93 N potassium hydroxide for a week at room temperature.

(8) Gray and Fuson, THIS JOURNAL, 56, 739 (1934).

(1) Ayres and Hauser, THIS JOURNAL, 65, 1095 (1943).

(2) Alexander, ibid., 69, 289 (1947).

(3) Westheimer, ibid., 58, 2209 (1936).

second order kinetics.[2] While this mechanism has been considered to involve the shift of a hydride ion,[9] we believe that the reactive intermediate is better described by a transition state involving at least four resonance structures (VIII).
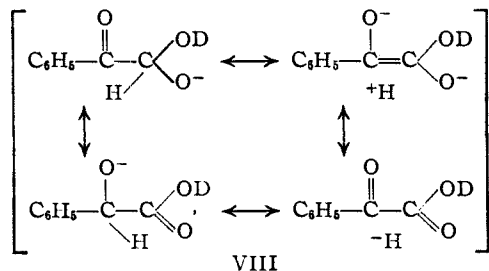
VIII

Experimental

Determination of C[13] in Benzoic Acid (VI).—A mixture of 0.0330 g. of benzoic acid containing an enriched content of C[13] in the carboxyl group, 0.25 cc. of purified chloroform and 0.25 cc. of concentrated sulfuric acid was introduced into a reaction vessel through which was passed continuously a slow stream of prepurified nitrogen, freed of carbon dioxide and saturated with dry chloroform at 45°. C. P. sodium azide (0.1036 g.) was tapped from a side-arm into the stirred, heated (40–44°) reaction mixture. The effluent gas was bubbled through two traps (separatory funnels) containing clear solutions of 0.26 N barium hydroxide. After thirty minutes, the precipitated barium carbonate was collected under nitrogen, washed with carbon dioxide-free water, and dried (29.3 mg., 55% yield).

Carbon dioxide for the mass spectrometric analyses was liberated from the barium carbonate in a standard sample conversion apparatus.[10] The abundance ratios of $C^{12}O_2$ to $C^{13}O_2$ were determined with a Nier-type mass spectrometer.[11] From a plot of the positive ion current against the accelerating voltage it was found that because of incomplete resolution ions of mass 44 ($C^{12}O_2^+$) contributed about 5% to the peak at mass 45 ($C^{13}O_2^+$). Consequently a correction of 5% was made on the averages of the observed abundance ratios.

Anal. Abundance ratio $C^{12}O_2/C^{13}O_2$: 39.7, 41.5, 41.8, 39.5, 38.9; 40.3 ± 1.1. Corrected for resolution: 42.3, corresponding to 2.32% $C^{13}O_2$.

Normal carbon dioxide abundance ratio: 81.8, 80.9, 81.2, 81.5: 81.4 ± 0.3. Corrected for resolution: 85.5, corresponding to 1.16% $C^{13}O_2$.

Preparation of Labeled Mandelic Acid (VI).—An ethereal solution of benzoyl chloride prepared from 0.3014 g. of benzoic acid (I) (2.32% C[13] in the carboxyl group) by treatment with thionyl chloride was added dropwise to an eight-fold excess of ethereal diazomethane[12] at −10 to −5°. After being sixteen hours at 4°, crude diazoacetophenone, recovered by evaporation of the solvent *in vacuo*, was dissolved in 50 cc. of anhydrous ether and treated with a dilute ethereal solution of bromine.[13] After the initially vigorous evolution of nitrogen and the development of a persistent red color, the reaction mixture was washed with sodium bisulfite and water. Crude ω,ω-dibromoacetophenone (V) obtained as a yellowish-amber oil by evaporation of solvent *in vacuo*, was converted to VII by refluxing for twenty-five minutes in 5% aqueous

potassium hydroxide.[14] The filtered reaction mixture was clarified with Norit-A, acidified with concentrated hydrochloric acid and extracted with four portions of ether. Evaporation of the dried ether solution gave crude mandelic acid which was recrystallized from benzene; 0.09 g. of light tan crystals; m. p. 112–114° (24% of the theoretical yield based on I). Two more recrystallizations afforded 0.0641 g. of purer VI, m. p. 117–118.5°, showing no depression on admixture with an authentic sample.

Determination of C[13] in Mandelic Acid (VII). (a) **Oxidation with Acidic Permanganate.**—A solution of 0.0627 g. of the mandelic acid obtained above (m. p. 117–118.5°) in 1.75 cc. of 10% sulfuric acid was oxidized[15] by 0.14 g. of potassium permanganate in the same apparatus used above for the Schmidt reaction, the nitrogen being purified by passing through two solutions of barium hydroxide. After the reaction mixture had been heated for ten minutes at 80–95°, the barium carbonate was collected as described above (0.1138 g., 140% yield).

Anal. Abundance ratio $C^{12}O_2/C^{13}O_2$: 78.3, 78.8, 78.5, 78.8, 78.6 ± 0.2. Corrected for resolution: 82.5 ± 0.2, corresponding to 1.20% $C^{13}O_2$.

From the reaction mixture 0.0365 g. (72.5% yield) of benzoic acid (IX), m. p. 122–123°, was isolated.[16]

(b) **Oxidation with Neutral Permanganate.**—The sublimed residues from the recrystallization of the mandelic acid (11.1 mg., m. p. 80–103°[17]) were dissolved in 0.36 cc. of water and oxidized with 0.05 g. of potassium permanganate, 8.3 mg. of barium carbonate being collected in the usual manner (57.5% yield).

Anal. Abundance ratio $C^{12}O_2/C^{13}O_2$: 81.0, 77.5, 78.5, 77.5, 76.6, 77.4: 78.1 ± 1.1. Corrected for resolution 82.0 ± 1.1, corresponding to 1.21% $C^{13}O_2$.

Pure benzoic acid, m. p. 121.6–122°, was isolated from the reaction mixture by extraction and sublimation.

(c) **Determination of C[13] in Benzoic Acid (IX).**—As in the previously described Schmidt procedure, 0.0350 g. of benzoic acid was decarboxylated to 18.2 mg. of barium carbonate (32.2% yield).

Anal. Abundance ratio $C^{12}O_2/C^{13}O_2$: 41.6, 41.5, 42.8, 41.6, 42.1, 40.7, 40.8: 41.6 ± 0.5. Corrected for resolution: 43.7 ± 0.5, corresponding to 2.24% $C^{13}O_2$.

Determination of Deuterium.—Essentially the procedure described by Cohn[18] was employed with minor modifications. For the extended procedure recommended for the purification of the water of combustion, we have substituted a single sublimation in order to permit analysis of smaller samples of organic material. This simplification has resulted in an increased error, deuterium-free compounds giving water apparently containing 0.02–0.04% deuterium oxide.

Rearrangement of Phenylglyoxal Hydrate to Mandelic Acid (X).—Phenylglyoxal was obtained as its hydrate, m. p. 74–77°, by the oxidation of acetophenone with selenium dioxide[19]; phenylosazone, m. p. 150.6–151.4°; reported[20] m. p. 151–2°.

Anal. Calcd. for $C_8H_6O_2 \cdot H_2O$: C, 63.10; H, 5.30. Found: C, 63.61; H, 5.76.

A cooled mixture (incompletely dissolved) of 0.587 g. of phenylglyoxal hydrate in 9.085 g. of water containing 7.25 weight per cent. of deuterium oxide (corrected for water of hydration) was shaken vigorously with 0.59 g.

(9) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940; p. 319, 351.

(10) Wilson, Nier and Reimann, "Preparation and Measurement of Isotopic Tracers," J. W. Edwards, Ann Arbor, Michigan, 1946, pp. 31–42 (Rittenberg).

(11) *Ibid.*, pp. 11–30 (Nier).

(12) Bradley and Robinson, *J. Chem. Soc.*, 1317 (1928).

(13) Houben–Weyl, "Die Methoden der organischen Chemie," Georg Thieme, Leipzig, 1941, Vol. IV, p. 883.

(14) Engler and Wöhrle, *Ber.*, **20**, 2202 (1887).

(15) Fieser, "Experiments in Organic Chemistry," D. C. Heath Co., Boston, Mass., 1944, 2nd ed., p. 219.

(16) The 140% yield of carbon dioxide may be explained by assuming the complete oxidation of only 5% of the mandelic acid. This amount of destructive oxidation would cause an error of +0.04% in the C[13] content of recovered carbon dioxide.

(17) Presumably contaminated by benzoic acid.

(18) Ref. 10, pp. 51–59.

(19) Blatt, "Organic Syntheses," John Wiley, New York, N. Y., 1939, Coll. Vol. II, p. 509.

(20) Müller and von Pechmann, *Ber.*, **22**, 2558 (1889).

of barium oxide. After twenty hours at 28°, the reaction mixture was acidified with concentrated hydrochloric acid and extracted with six 10-cc. portions of ether. Evaporation gave 0.425 g. (72.5%) of crystalline mandelic acid which was dissolved in 10 cc. of 0.5 N barium hydroxide. The solution was filtered, allowed to stand one hour, acidified, and extracted with ether. After repetition of the equilibration and sublimation, 0.317 g. (54.2%) of mandelic acid was obtained. Recrystallized from benzene, pure X was obtained, m. p. 118.5–119.3°, showing no depression on admixture with an authentic sample.

Anal. Calcd. for $C_8H_7D_{(7.25\%)}O_3$: D$_2$O, 0.906. Found: D$_2$O, 0.036.

The above procedure was repeated using 10.24 g. of water containing 27.6 weight per cent. (corrected for water of hydration) of deuterium oxide and 0.61 g. of phenylglyoxal hydrate. There was obtained 0.360 g. (59%) of crude mandelic acid. Recrystallization afforded 0.296 g., m. p. 118–119°.

Anal. Calcd. for $C_8H_7D_{(27.6\%)}O_3$: D$_2$O, 3.45. Found: D$_2$O, 0.039.

α-Hydroxyphenylacetic-*d* Acid.—Mandelic acid (1.470 g.) was refluxed under nitrogen for one week with 13.52 g. of 29.56% deuterium oxide and 1.23 g. of barium oxide. The deuterated mandelic acid, recovered by acidification with concentrated hydrochloric acid, extraction with ether and evaporation *in vacuo*, was equilibrated twice by re-

fluxing for eighteen hours with 17 cc. of water under nitrogen. The recovered equilibrated acid was recrystallized from benzene giving a first crop (A) weighing 0.876 g.

Anal. Calcd. for $C_8H_7D_{(29.56\%)}O_3$: D$_2$O, 3.70. Found: D$_2$O, 3.57.

Sample A was twice reequilibrated by treating with 23 cc. of 0.5 N baryta for seventy-five minutes at room temperature.

Anal. Found: D$_2$O, 3.57, 3.57, 3.57.

Summary

Using phenylglyoxal in which the ketone carbon is marked with C^{13}, it has been proved that there is no rearrangement of the carbon skeleton in the alkali-catalyzed conversion to mandelic acid. The failure of solvent deuterium to become attached to the alcohol carbon atom of mandelic acid prepared from phenylglyoxal in heavy water has allowed exclusion of a proton-removal mechanism and has substantiated a mechanism involving intramolecular transfer of hydrogen. The present status of the mechanism is discussed.

Configuration and Adsorption. A Comparison of the Adsorption of the *cis* and *trans* Isomers of Dichloroethylene on Activated Carbon

BY DAVID H. VOLMAN AND LAWRENCE J. ANDREWS

In an attempt to account for the data of adsorption from the vapor phase on activated carbon adsorbates may be separated into three classifications: first, molecules which can undergo hydrogen bonding; second, molecules which do not form hydrogen bonds but which possess permanent dipole moments; third, molecules which do not form hydrogen bonds and do not have permanent dipole moments.

Only the first classification is known definitely to behave abnormally in adsorption on carbon. For this type of compound the correlation of adsorbability and condensation properties of the gas has been pointed out recently by Volman and Klotz.[1] It was proposed that the initial adsorption does not reflect the hydrogen bonding properties of the molecule even though the relative pressures do, and the apparent anomalies in adsorption are to be explained by the values assigned to the relative pressure axis for the isotherms. For both of the other classifications no anomalies comparable to those found with a compound of the first classification such as water are known. However, it seemed of interest to determine the effect of the existence of a permanent dipole moment on van der Waals adsorption on carbon. A near approach to a comparison of this nature should be obtained by studying the adsorption of molecules differing only in geometric configura-

tion. Thus by choosing *cis*- and *trans*-dichloroethylene the principal difference in interaction effects would seem to be the large difference in dipole moment, zero for the *trans* and 1.8 debyes for the *cis* compound.[2] In addition the isomers are easily obtained in a pure state and have convenient physical properties for adsorption studies.

Further interest in the problem derives from the fact that no comparisons of the adsorption of *cis–trans* isomers from the vapor phase have been made. However, in recent years extensive studies directed toward the separation of *cis–trans* isomers by chromatographic adsorption have been carried out.[3] These studies have all been made from solution and primarily with stereoisomers of carotenoids. In addition the adsorption of maleic and fumaric acids from aqueous solution on activated carbon has been carried out.[4] Here the adsorption is mainly dependent on the degree of ionization of the acids in solution. It was expected that a study of gas phase adsorption of *cis–trans* isomers would yield information on the possibility of separation of such isomers by adsorption techniques.

Experimental

Preparation of Materials.—The *trans* compound was obtained by fractionation of Eastman Kodak Co. *trans-*

(1) Volman and Klotz. *J. Phys. Chem.*, **14**, 642 (1946).

(2) *Trans. Faraday Soc.*, **30**, Appendix (1934).

(3) Zechmeister, *Chem. Rev.*, **34**, 267 (1944).

(4) Phelps. *J. Chem. Soc.*, 1724 (1929).