[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

THE REARRANGEMENT OF THE 3-C-PHENYLTRIOSES

LEE IRVIN SMITH AND RAY H. ANDERSON[1]

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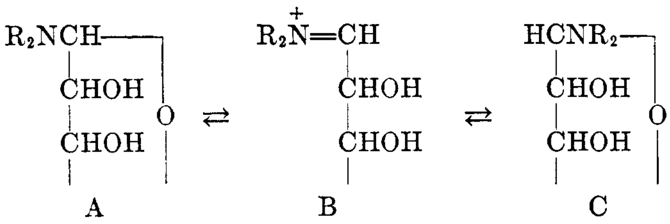
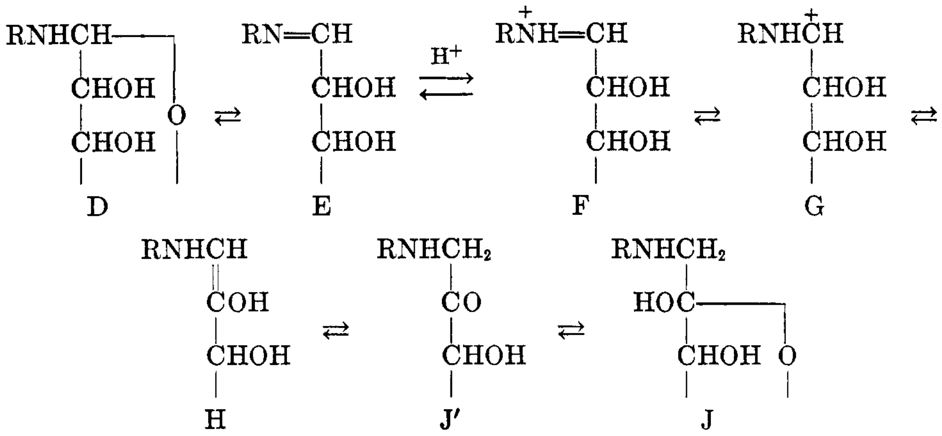
When primary or secondary amines react with aldopentoses or aldohexoses, the initial products are glycosylamines. Certain of these glycosylamines—those derived from primary amines and from secondary *aliphatic* amines—undergo mutarotation in solution, probably *via* a Schiff base or the cation of a Schiff base (A → B → C).



Glycosylamines derived from secondary *aromatic* amines do not undergo mutarotation, and it has been suggested (1) that the reason for this lies in the very weak basicity of the nitrogen atom in these compounds—*i.e.*, cation B is not formed. All glycosylamines are unstable toward acids (1–4), although the stability in water varies widely. Moreover, glycosylamines derived from *primary, aromatic* amines (D)—and only these—will undergo Amadori rearrangement to isoaminoglycosides (J) (5). Weygand (5) has suggested that this rearrangement involves stages D to J inclusive.



The trioses glyceraldehyde and dihydroxyacetone, under certain conditions, rearrange to methylglyoxal with loss of the elements of water (6). In dilute acetic

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[1] Abstracted from a thesis by Ray H. Anderson, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, July, 1950.

acid, glyceraldehyde is converted into methylglyoxal only in the presence of a *primary aromatic* amine, whereas dihydroxyacetone in the same solvent forms the ketoaldehyde whether or not an amine is present. Thus there is a certain similarity between the conditions for this transformation of glyceraldehyde and those required for the Amadori rearrangement.

Because of the complexity of the reactions which may occur between aqueous solutions of simple sugars and amines, it appeared worthwhile to investigate this reaction for some simple isomeric sugars in which one of the carbon atoms was marked, and in which the reactions would not be complicated by the opening and closing of furanose or pyranose rings. Chosen for this purpose were the three 3-C-phenyltrioses: β-phenylglyceraldehyde (I), α,β-dihydroxypropiophenone (II), and phenyldihydroxyacetone (III). The behavior of these three substances, in dilute acetic acid, was studied with and without the inclusion of amines in the solution.

$$\underset{\text{I}}{C_6H_5CHOHCHOHCHO} \qquad \underset{\text{II}}{C_6H_5COCHOHCH_2OH} \qquad \underset{\text{III}}{C_6H_5CHOHCOCH_2OH}$$

Reaction of β-phenylglyceraldehyde (I) with excess aniline in aqueous solution led to an oily, yellow Schiff base (IV) which was unstable at room temperature. When I was present in excess, a white, solid bis-compound V was formed. The primary products IV and V

$$\underset{\text{IV}}{C_6H_5CHOHCHOHCH{=}NC_6H_5} \qquad \underset{\text{V}}{(C_6H_5CHOHCHOHCHOH)_2NC_6H_5}$$

$$\underset{\text{VI}}{C_6H_5CH_2COCHO}$$

were insoluble in water. In studying the further transformations of I, IV, and V, sufficient dioxane was added to the solutions to prevent precipitation of IV and V.

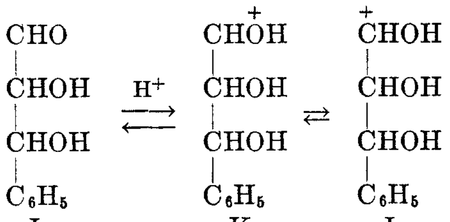
In solution in dilute acetic acid and dioxane, both substances IV and V were transformed into benzylglyoxal (VI). In the same solvent mixture, I was also transformed into the glyoxal VI, but only in the presence of a primary aromatic amine (aniline, *m*-nitroaniline, *p*-toluidine, *o*-toluidine): under these circumstances, transformation of I into VI occurred to the extent of at least 66% in 72 hours at room temperature. Other types of amines—diphenylamine, methylaniline, ethanolamine, ethylamine, amylamine, phenylalanine ester, glycine ester, glycine, diethylamine, *n*-ethylethanolamine—were without effect. Presence of VI in these solutions of I, IV, or V was indicated by precipitation of the *m*-nitrobenzoylosazone of VI when *m*-nitrobenzoylhydrazide was added to the solutions but in order to be certain that VI was actually present, a solution of I and aniline in dilute acetic acid was distilled with steam. Benzylglyoxal VI was isolated from the distillate and identified by comparison with an authentic specimen of VI.

Both of the ketotrioses II and III were transformed, in dilute acetic acid, into acetylbenzoyl (VII) with loss of the elements of water.

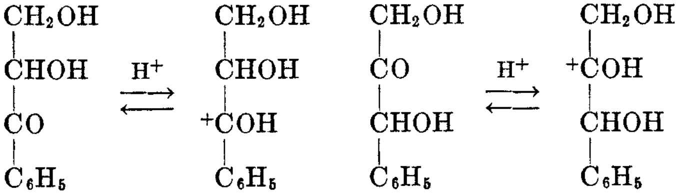
$$\underset{\text{VII}}{C_6H_5COCOCH_3}$$

Although the transformations of II and III took place at a rate of only about 25% of that of I, the transformations of II and III occurred even if no amine were present in the solution. The only change brought about by addition of aniline to solutions of II and III in dilute acetic acid was a slight increase in the rate of the transformation of these substances into VII.

These data concerning the rearrangement of the phenyltrioses can be interpreted quite well on the basis of Weygand's outline of the Amadori rearrangement (5). The key intermediate is a cation such as G; unless this is formed, the reaction will stop at stage F. This fact gives a possible explanation for the requirement of the presence of a primary aromatic amine in order that the aldotriose may rearrange, whereas it is not a necessary requirement for the rearrangement of a ketotriose. Thus, the equilibrium for the aldose (I, K, L) is unfavorable to the formation of the secondary cation L, but in the case of the ketoses, the equilibria, leading respectively to the tertiary cations M and N are more favorable.



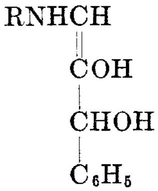
$$\underset{\text{I}}{CHO-CHOH-CHOH-C_6H_5} \overset{H^+}{\rightleftarrows} \underset{\text{K}}{CH\overset{+}{O}H-CHOH-CHOH-C_6H_5} \rightleftarrows \underset{\text{L}}{\overset{+}{C}HOH-CHOH-CHOH-C_6H_5}$$



$$\underset{\text{II}}{CH_2OH-CHOH-CO-C_6H_5} \overset{H^+}{\rightleftarrows} \underset{\text{M}}{CH_2OH-CHOH-{}^+COH-C_6H_5} \qquad \underset{\text{III}}{CH_2OH-CO-CHOH-C_6H_5} \overset{H^+}{\rightleftarrows} \underset{\text{N}}{CH_2OH-{}^+COH-CHOH-C_6H_5}$$

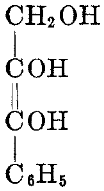
In the case of aldoses, the presence of an amine results in the formation of E and then F, and so to a favorable equilibrium as far as F, but G cannot form unless the charge can be transferred from the nitrogen to the carbon (F → G) to a sufficient degree that the subsequent steps of the reaction may occur. This means that the amine must be one giving a Schiff base (E) of just the proper basicity so that the change F → G may occur, and it has been found that a primary aromatic amine satisfies these requirements.

The next step, in all cases, appears to be the expulsion of a proton, resulting in the formation of H from G, O from M, and O and/or (unlikely) P from N.



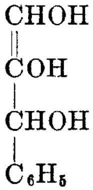
$$RNHCH=COH-CHOH-C_6H_5$$

H



$$CH_2OH-COH=COH-C_6H_5$$

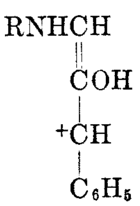
O



$$CHOH=COH-CHOH-C_6H_5$$

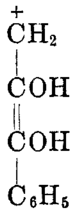
P

In those cases (pentoses, hexoses) in which a tautomeric shift of H may lead to a compound capable of undergoing ring closure to a furanose or pyranose form, these changes may occur (H → J′ → J) and Amadori rearrangement results. It may be that the ability of J′ to undergo ring closure is the determining factor in whether or not Amadori rearrangement occurs, but this cannot be said with certainty. In any event, if the change H → J′ → J does not occur, the next step appears to be elimination of the β (allylic?) hydroxyl group (5, 7) producing new cations Q, R, S (= Q) from H, O, and P respectively.



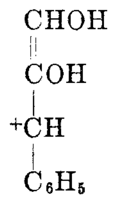
$$\begin{array}{c}\text{RNHCH}\\ \|\\ \text{COH}\\ |\\ {}^{+}\text{CH}\\ |\\ \text{C}_6\text{H}_5\end{array}$$

Q



$$\begin{array}{c}\overset{+}{\text{C}}\text{H}_2\\ |\\ \text{COH}\\ \|\\ \text{COH}\\ |\\ \text{C}_6\text{H}_5\end{array}$$

R



$$\begin{array}{c}\text{CHOH}\\ \|\\ \text{COH}\\ |\\ {}^{+}\text{CH}\\ |\\ \text{C}_6\text{H}_5\end{array}$$

S

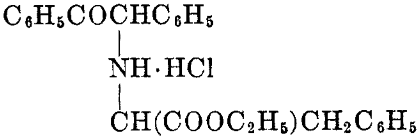
These new cations, by tautomeric shifts and expulsion of a proton (also hydrolysis in the case of Q) lead to benzylglyoxal (VI) from Q and S and to acetylbenzoyl VII from R. That acetylbenzoyl (VII) was produced from both ketoses II and III shows that expulsion of a proton from cation N (derived from III), though it might have occurred in two ways, occurred in one way only—the proton was eliminated from the carbon atom next to the phenyl group leading to O, R, and then VII and not to benzylglyoxal (VI) *via* P and S.

As a preliminary to this study of the reactions of the phenyltrioses, the reaction between a simple ketol, benzoin, and an amino ester, phenylalanine ethyl ester, was studied. Previously, condensation of benzoin had been reported in the case of aromatic amines only (8, 9); in every case an aminoketone was produced

$$C_6H_5COCHOHC_6H_5 + RNH_2 \rightarrow C_6H_5COCH(NHR)C_6H_5$$

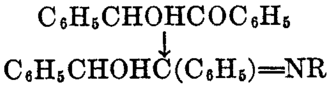
Recently Lutz, Freek, and Murphy (10) reported the formation of aminoketones from benzoin and aliphatic amines when phosphorus pentoxide was used as the condensing agent.

By use of a modification of the procedure of Lutz, *et al.*, a stable, crystalline hydrochloride VIII was obtained from benzoin and phenylalanine ethyl ester.



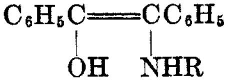
$$\begin{array}{l}C_6H_5COCHC_6H_5\\ \qquad\quad\;\; |\\ \qquad\quad\;\; NH\cdot HCl\\ \qquad\quad\;\; |\\ \qquad\quad\;\; CH(COOC_2H_5)CH_2C_6H_5\end{array}$$

VIII



$$\begin{array}{c}C_6H_5CHOHCOC_6H_5\\ \downarrow\\ C_6H_5CHOHC(C_6H_5){=}NR\end{array}$$

IX R = $-CH(COOC_2H_5)CH_2C_6H_5$



$$\begin{array}{ccc}C_6H_5C & = & CC_6H_5\\ | & & |\\ OH & & NHR\end{array}$$

X R as in IX

The hydrochloride melted at 174–176°, and from it the crystalline base, melting at 104–105°, was obtained. This base was stable at 0°, but was unstable when kept at room temperature.

The formation of this condensation product may be regarded as occurring *via* the mechanism discussed above for the reaction between hydroxycarbonyl compounds and amines. The initial step involves formation of the Schiff base IX (corresponding to E); this leads to the cations corresponding to F and G. A proton is expelled from the latter, leading to the enol X which then undergoes a tautomeric shift, forming VIII. It should be noted that, if this mechanism is correct, the carbonyl group in the product VIII is not the one present originally in the benzoin molecule, for this mechanism leads to a compound in which the original carbonyl group has been "reduced" whereas the alcohol group has been "oxidized", *i.e.*, a sort of Amadori rearrangement. This point, however, was not examined experimentally.

EXPERIMENTAL PART[2]

Cinnamaldehyde diethyl acetal (96.5 g., 81%) was prepared from cinnamaldehyde (66 g.) and ethyl orthoformate (82 g.) in ethanol (87 g.) as described by Claisen (11). The product boiled at 120–123°/3 mm., n_D^{25} 1.5121.

β-Phenylglyceraldehyde diethyl acetal. It was not possible to duplicate the preparation of this substance from cinnamaldehyde acetal as described by Fischer and Hoffa (12). Invariably *black* manganese hydroxide separated, and no hydroxylation occurred (13). Hydroxylation was successful, however, when the method of Rüber was used (14). A solution of cinnamaldehyde acetal (25.4 g.) in ethanol (1.5 l.) was cooled to −40° and held at that temperature and stirred vigorously while a solution of potassium permanganate (24 g.) in water (800 cc.) was slowly (4 hours) added. The mixture was allowed to attain room temperature and the *brown* manganese dioxide was removed. The filtrate, after concentration under reduced pressure to a volume of 200 cc., was extracted with four 100-cc. portions of ether. The combined extracts were dried and the solvent was removed. The residual yellow oil (16 g., soluble in ether and ethanol, sparingly soluble in petroleum ether) was dissolved in boiling petroleum ether (3 l.), and the solution was cooled (0°). After one hour, an oil (6 cc.) separated; the supernatant liquid was decanted and again cooled (0°). The oil was dissolved in boiling petroleum ether (1 l.) and this solution was cooled (0°). Both solutions deposited crystalline material after about an hour. The solid was removed from the combined solutions and recrystallized from petroleum ether. It then weighed 6 g. (13%) and melted at 38°. In another experiment, double quantities of materials were used; in this case, the product weighed 20 g., (21%) and melted at 38°.

Anal. Calc'd for $C_{13}H_{20}O_4$: C, 65.06; H, 8.33.
Found: C, 64.80; H, 8.21.

β-Phenylglyceraldehyde (I). The above acetal (5 g.) was stirred rapidly with aqueous sulfuric acid (50 cc., 0.5%) until the mixture became homogeneous. Excess barium carbonate was added, the mixture was filtered and the filtrate was set aside at room temperature. After several hours, the solid was removed, washed with cold water, crystallized from a mixture of dioxane and petroleum ether, and dried at 85° under reduced pressure for two days. It then weighed 2.5 g. (70%), sintered at 118°, and melted at 123–125°. The melting point and the composition of this material depended upon the length of time, etc., it was dried; it was not possible to obtain it in anhydrous form. These properties were observed previously by Fischer and Hoffa (12). The substance reduced Fehling's solution, and Tol-

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[2] Microanalyses by R. W. Amidon, Jay S. Buckley, William Cummings, R. E. Kelly, and H. W. Turner.

lens' reagent at room temperature and it formed a phenylhydrazone which, after crystallization from ethanol, melted at 167–168° [reported m.p. 170° (12)]. The substance gave poor analytical values, as observed by Fischer and Hoffa (12).

Anal. Calc'd for $C_9H_{10}O_3$: C, 65.06; H, 6.03.
Found: C, 63.64; H, 6.62.

Schiff base (IV). A cold solution of I (0.5 g.) in water (20 cc.) was added, slowly and with stirring, to a cold solution of excess (200%) aniline (1 g., distilled from zinc dust) in water (20 cc.) containing acetic acid (1 cc.). A yellow oil separated immediately; this was removed, washed with water, taken up in ether, and the ethereal solution was dried. Removal of the solvent left IV as a yellow oil (0.45 g., 65%).

Anal. Calc'd for $C_{15}H_{15}NO_2$: C, 74.70; H, 6.06; N, 5.81.
Found: C, 74.56; H, 6.82; N, 6.04.

This material was not stable; after several days at room temperature, it became dark and viscous; satisfactory analytical values were difficult to obtain. It reduced Fehling's solution, Tollens' solution, and an alkaline solution of methylene blue at room temperature. Action of dilute (5%) hydrochloric acid upon IV resulted in immediate production of aniline.

Bis-compound (V). A cold solution of aniline (0.3 g., 0.003 mole) in water (20 cc.) containing acetic acid (1 cc.) was added, slowly and with stirring, to a cold (0°) solution of I (0.5 g., 0.003 mole) in water (20 cc.). After 15 minutes, the white solid was removed and washed with cold water. The product was dried under reduced pressure at room temperature, when it weighed 0.4 g. (60%), m.p. 59–64°. It decomposed at temperatures above about 20°; it could not be recrystallized, for warm solutions of it in alcohol or dioxane either with or without a little acetic acid, deposited a brown tar in a short time.

Anal. Calc'd for $C_{24}H_{27}NO_6$: C, 67.76; H, 6.40; N, 3.30.
Found: C, 67.82; H, 6.97; N, 3.16.

Benzylglyoxal (VI) (2.3 g., 6%) was prepared from benzyl chloride (31 g.) as described by Dakin (15). The *p*-nitrophenylosazone melted at 276–280°; Dakin reported m.p. 275–280°. When VI (0.2 g.) in acetic acid (1 cc.) and dioxane (5 cc.) was added to a solution of *m*-nitrobenzhydrazide (0.5 g.) in dioxane (5 cc.) and water (10 cc.), the solution, after standing for three days, deposited the *m*-nitrobenzoylosazone of VI. This material, after crystallization from hot dioxane, weighed 0.34 g. (57%), m.p. 190–192°.

Anal. Calc'd for $C_{23}H_{18}N_6O_6$: C, 58.22; H, 3.80; N, 17.72.
Found: C, 58.14; H, 3.88; N, 17.60.

Rearrangement of IV *and* V. The Schiff base IV (0.2 g.) in purified (16) dioxane (1 cc.) was added to a solution of *m*-nitrobenzhydrazide (0.4 g.) in acetic acid (1 cc.), water (5 cc.), and dioxane (4 cc.). After three days at room temperature, the solid was crystallized from dioxane and dried at 100° under reduced pressure. It weighed 0.18 g. (45%), and melted at 187–189° alone or when mixed with the *m*-nitrobenzoylosazone of VI. In a duplicate experiment, but using V (0.2 g.), the product weighed 0.15 g. (32%) and melted at 187–189°, alone or when mixed with the product from IV.

Rearrangement of I. A solution of I (0.5 g.), aniline (1 g.), and *m*-nitrobenzhydrazide (2 g.) in dioxane (10 cc.) and acetic acid (1 cc.) deposited no precipitate after three days at room temperature. Addition of water (10 cc.) brought about deposition of solid within three days; this material (0.97 g., 66%) melted at 188–190° alone or when mixed with the product from either IV or V.

Anal. Calc'd for $C_{23}H_{18}N_6O_6$: C, 58.22; H, 3.80; N, 17.72.
Found: C, 58.39; H, 4.02; N, 17.59.

This experiment was repeated with changes and results as follows: Omission of *either* aniline or acetic acid resulted in no deposition of solid after six days; substitution of *p*-toluidine, *o*-toluidine, or *m*-nitroaniline for aniline led in each case to the *m*-nitrobenzoylosazone of VI as shown by mixture melting point; substitution of aniline by diphenylamine, methylaniline, ethanolamine, ethylamine, amylamine, phenylalanine ethyl ester, glycine ethyl ester, glycine, diethylamine, or N-ethylethanolamine led in each case to no deposition of solid after six days.

A solution of I (0.3 g.) in water (20 cc.) was added dropwise (20 minutes) and with stirring to a solution of aniline (0.4 g.) in water (5 cc.) containing acetic acid (0.5 cc.). The temperature was maintained at 5° during addition, and the solution was maintained at 0° for one hour afterward. The solution was extracted twice with 25-cc. portions of ether, the combined extracts were dried, and the solvent was removed under reduced pressure at room temperature. The residual yellow oil was stirred into cold water (50 cc.) containing acetic acid (1 cc.) and the mixture was distilled with steam until the oil became a brown tar. About 0.04 g. of white crystalline material collected in the condenser; this melted at 119–121° alone or when mixed with VI.

Anal. Calc'd for $C_9H_8O_2$: C, 72.97; H, 5.41.

Found: C, 72.96; H, 5.58.

This material gave a *p*-nitrophenylosazone melting at 273–277°, as reported by Dakin (15).

β-Chloropropiophenone (24 g., 60%) was prepared from benzene and β-chloropropionyl chloride (30 g.), as described by Hale and Britton (17).

Vinyl phenyl ketone (18). β-Chloropropiophenone (12 g.) was added to a hot solution of potassium acetate (6 g., freshly fused) in ethanol (100 cc.). The mixture was cooled to room temperature and was filtered. The filtrate, containing the vinyl phenyl ketone (theoretical yield, 9 g.) was used immediately for the next step.

α,β-Dihydroxypropiophenone (II). The above filtrate was diluted to 700 cc. with ethanol, cooled to −40°, and potassium permanganate (12 g.) in water (400 cc.) was added slowly (four hours) with vigorous stirring. The mixture was allowed to come to room temperature, the *brown* manganese dioxide was removed, and the filtrate, concentrated to 100 cc. under reduced pressure, was extracted with four 50-cc. portions of ether. The combined extracts were dried, concentrated to 20 cc., diluted with petroleum ether (10 cc.), and placed in a refrigerator at 0° for a day. The solid was crystallized from a mixture of ether and petroleum ether. It weighed 2.8 g. (25%) and melted at 80°. It reduced Fehling's solution, and an alkaline solution of methylene blue at room temperature.

Anal. Calc'd for $C_9H_{10}O_3$: C, 65.06; H, 6.03.

Found: C, 65.27; H, 6.35.

The *p-nitrophenylhydrazone*, crystallized from aqueous ethanol, was orange-brown, m.p. 171–173°.

Anal. Calc'd for $C_{15}H_{15}N_3O_4$: C, 59.80; H, 4.98; N, 13.95.

Found: C, 60.08; H, 5.26; N, 13.81.

Acetylbenzoyl (VII) (14 g., 62%) was prepared from isonitrosopropiophenone (25 g.) as described by Hartman and Roll (19).

The *m-nitrobenzoylosazone*, prepared from VII (0.2 g.) and *m*-nitrobenzhydrazide (0.5 g.) in aqueous dioxane containing acetic acid, weighed 0.3 g. (50%). After crystallization from ethanol, the substance melted at 186–187°.

Anal. Calc'd for $C_{23}H_{18}N_6O_6$: C, 58.22; H, 3.80; N, 17.72.

Found: C, 58.33; H, 3.92; N, 17.56.

Acetylmandeloyl chloride (20 g., 69%) was prepared from mandelic acid (21 g.) as described by Thayer (20).

Acetylmandeloyldiazomethane. Acetylmandeloyl chloride (6 g.) in ether (20 cc.) was added, dropwise and with stirring, to a cold (0–5°) solution of diazomethane [from 12 g. of nitrosomethylurea (21)] in ether (170 cc.). The mixture was allowed to stand at room temperature for four hours, then was concentrated to a volume of 20 cc., and kept at 0° for four hours. The solid diazoketone was removed, washed with cold ether, and crystallized from a mixture of dioxane and petroleum ether. The slightly yellow product weighed 3.2 g. (60%), m.p. 48–50°. It decomposed on standing in a vacuum desiccator for three days at room temperature, and was not analyzed.

Phenyldihydroxyacetone diacetate. A solution of the diazoketone (2 g.) in acetic acid (25 cc.) containing a trace of cupric acetate (40 mg.) was heated to the boiling point (22). After the evolution of gas subsided, the solution was concentrated under reduced pressure at 50° to a volume of 5 cc. and then diluted with chloroform (40 cc.). This solution was washed three times with water, dried, and evaporated under reduced pressure. The residual sirup was dissolved in acetic anhydride (25 cc.) containing zinc chloride (0.3 g.); the solution was allowed to stand overnight and was then poured into ice-water (100 cc.). The mixture was extracted with ether, the extract was dried, and the solvent was evaporated. The semi-solid residue was recrystallized from a mixture of dioxane and petroleum ether. The diacetate weighed 0.5 g. (25%), m.p. 39–41°.

Anal. Calc'd for $C_{13}H_{14}O_5$: C, 62.40; H, 5.65.
Found: C, 62.56; H, 5.48.

Phenyldihydroxyacetone (III). A cold (0°) solution of barium hydroxide octahydrate (2 g.) in water (10 cc.) was added, with rapid stirring, to a cold (0°) solution of the above diacetate (0.5 g.) in water (10 cc.) and ethanol (10 cc.). The mixture was stirred at 0° for two hours, and was then saturated with carbon dioxide. The solid was removed, and the filtrate, when allowed to stand in an open beaker at room temperature for two days, deposited a crystalline solid. This was crystallized from aqueous ethanol; weight, 0.21 g. (60%); m.p. 71–73°, reduces Fehling's solution or an alkaline solution of methylene blue at room temperature. A mixture of III with II (m.p. 80°) melted at 66–70°.

Anal. Calc'd for $C_9H_{10}O_3$: C, 65.06; H, 6.03.
Found: C, 65.06; H, 6.22.

The *p-nitrophenylhydrazone*, crystallized from aqueous ethanol, melted at 162–164°. A mixture of this with the *p*-nitrophenylhydrazone of II (m.p., 171–173°), melted at 154–159°.

Anal. Calc'd for $C_{15}H_{15}N_3O_4$: C, 59.80; H, 4.98; N, 13.95.
Found: C, 59.94; H, 4.81; N, 13.81.

Rearrangement of II. Water (2 cc.) was added to a solution of II (0.1 g.) and *m*-nitrobenzhydrazide (0.4 g.) in dioxane (2 cc.) containing acetic acid (0.2 cc.), and the mixture was allowed to stand at room temperature. After three days, 0.05 g. of solid had separated; after ten days, no further solid separated, and the total amount of solid was 0.14 g. The experiment was duplicated except that aniline (0.2 g.) was added to the solution. After three days the solid weighed 0.07 g., and after ten days the total precipitate weighed 0.17 g. The solids from these experiments melted at 183–186°, alone or when mixed. After crystallization from dioxane, the material melted at 185–187°, alone or when mixed with the *m*-nitrobenzoylosazone of acetylbenzoyl (VII). The solid from either experiment, when mixed with the *m*-nitrobenzoylosazone (m.p. 190–192°) of benzylglyoxal (VI) melted at 178–184°.

Rearrangement of III. The experiments reported for the rearrangement of II were duplicated exactly, substituting III for II. In the experiment in which no aniline was added, the precipitates after three and ten days weighed 0.04 g. and 0.13 g., respectively. In the experiment in which aniline was added, the precipitates after three and ten days weighed 0.06 g. and 0.15 g., respectively. These solids melted at 174–178°, alone or when mixed. After crystallization twice from a mixture of nitrobenzene and toluene, the solids melted at 184–186°, alone or when mixed with each other or with the *m*-nitrobenzoylosazone (m.p. 186–187°) of acetylbenzoyl (VII). When mixed with the *m*-nitrobenzoylosazone (m.p. 190–192°) of benzylglyoxal (VI) either solid melted at 175–180°.

Phenylalanine ethyl ester (6.8 g., 58%) was prepared from DL-phenylalanine (10 g.) as described by Fischer (23).

Reaction of benzoin with phenylalanine ethyl ester. Benzoin (2.3 g.), the ester (2.3 g.), and phosphorus pentoxide (0.15 g.) were mixed and the mixture was heated for one hour under reduced pressure (10). The mixture was cooled, stirred with dry ether (20 cc.), the ether solution was decanted, and to it was added, with rapid stirring, a solution of hydrogen chloride in ether (10 cc., 12%). The white, granular hydrochloride (2.5 g., 50%) was crystallized twice from a mixture of ethanol and ether; weight, 1.5 g.; m.p. 167–169°.

Anal. Calc'd for $C_{25}H_{26}ClNO_3$: C, 70.92; H, 6.19; N, 3.30.
Found: C, 70.60; H, 6.31; N, 3.22.

The above hydrochloride (0.5 g.) was shaken under nitrogen with aqueous sodium carbonate (50 cc., 10%) until the crystalline material became amorphous and then was extracted with ether (50 cc., peroxide-free). The extract was dried, evaporated to 20 cc. under reduced pressure at room temperature, diluted with petroleum ether (10 cc.), and set aside at −15°. After a day the product (0.15 g., m.p., 96–99°) was crystallized from a mixture of ethanol and ether, when it melted at 104–106°. Both the amino ketone and its hydrochloride were unstable at room temperature, but were stable at 0°. The analytical sample of the amino ketone was dried at 0° under reduced pressure for two days.

Anal. Calc'd for $C_{25}H_{25}NO_3$: C, 77.52; H, 6.51; N, 3.62.
Found: C, 77.36; H, 6.40; N, 3.84.

SUMMARY

1. The preparation of the three phenyltrioses has been described, and these substances have been characterized.

2. The rearrangement of these substances, in dilute acetic acid, with and without the inclusion of amines, has been studied. The phenylaldotriose was converted into benzylglyoxal, but only in the presence of a primary, aromatic amine. The phenylketotrioses were converted into acetylbenzoyl, and the presence of an amine was not required for this transformation to occur.

3. A mechanism has been suggested to account for these reactions.

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