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A preparation of phenylacetone.

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Thesis

A PREPARATION OF PHENYLACETONE

By

Lewis Terry
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INTRODUCTION

In this laboratory, condensation of naphthalene and chloroacetone in the presence of anhydrous aluminum chloride to form naphthylacetone was unsuccessful(1). Consequently, the synthesis of phenylacetone by the condensation of benzene with chloroacetone in the presence of aluminum chloride was undertaken. The two reactions, although different in certain respects, are essentially of the same type, and it was expected if the latter could be successfully effected, some hope might be held for the former.

Phenylacetone has been prepared by distilling a mixture of the barium(2) or calcium(3) salts of phenylacetic and acetic acids, and by passing the vapors of these acids over a heated thorium oxide catalyst(4). It has been prepared by the reaction of phenylacetyl chloride with zinc methyl(5), by rearrangement of alpha-phenyl beta-methyl ethylene oxide(6), by heating alpha-phenyl beta-methyl ethylene

(1) Chamberlin, Master of Arts Thesis (1937)

(2) Radziszewski, Berichte 3, 198 (1870)

(3) Young, J. Chem. Soc. 59, 621 (1891)

(4) Pickard and Kenyon, J. Chem. Soc. 105, 1124 (1914)

(5) Popow, Berichte 5, 500 (1872)

(6) Fournneau and Tiffeneau, Compt Rend. 141, 663 (1905)

glycol with dilute sulfuric acid(7), and by the hydrolysis of alpha-phenyl acetoacetic ester(8), or of phenacyl-malonic ester(9). It has been prepared from acetyl chloride and benzyl cadmium(10), also from acetyl chloride and sodium alpha-phenyl alpha-bromo-magnesium acetate(11). It has been formed when dry potassium hydroxide is allowed to act on an ether solution of alpha-phenyl alpha-chloro-acetone(12), when benzyl methyl allyl carbinol is distilled(13), and by a molecular rearrangement of beta-phenyl propylene followed by oxidation in the presence of mercuric oxide(14). According to a German Patent it has been obtained by passing certain aromatic dihydric alcohols over catalysts containing one or more of the heavy metals of groups one and eight of the periodic table(15). The catalyst preferably contains copper (specific compound not given). The reaction of phenylacetic acid and acetic

(7) Tiffeneau, Ann. Chim. 18, 10, 345, 368 (1907)

(8) Beckh, Berichte 31, 3163 (1898)

(9) Metzner, Ann. 298, 378 (1897)

(10) Gilman and Nelson, Rec. Trav. Chim. 55, 518 (1936)

(11) Ivanoff and Nicoloff, Bull. Soc. Chim. 51, 1325 (1932)

(12) Richard, Compt. Rend. 200, 1944 (1935)

(13) Grignard and Chambret, Compt. Rend. 182, 299 (1926)

(14) Tiffeneau, Compt. Rend. 134, 1506

(15) Farbenind, Chem. Abst. 24, 2140 (1930)

anhydride in the preparation of dibenzyl ketone yields 16% of phenylacetone(16). It is obtained when alpha-phenyl alpha-methyl ethylene glycol is heated to 550° C.(17).

Chamberlin(1), in this laboratory, obtained phenylacetone by adding chloroacetone to a mixture of benzene and anhydrous aluminum chloride and refluxing for four hours. The yield calculated on the basis of chloroacetone was 21.2%. This paper is a continuation of the work on this reaction in an effort to improve the yield of phenylacetone.

(16) Hurd and Thomas, J. Am. Chem. Soc. 58, 1240 (1936)

(17) Ramart-Lucas and Salmon-Legagneur, Bull. Soc. Chim.
51, 1669 (1932)

EXPERIMENTAL PART

The following procedure is general; individual runs are reported in separate paragraphs along with modifications of this procedure and the reasons for the modifications.

A 500 cc. three-neck flask was provided with a mercury seal stirrer, a water condenser, and a small addition funnel. The condenser was connected to a double trap of concentrated sulfuric acid, and a gas absorption bottle was connected to the trap.

Thirty-four grams (.26 mols) of anhydrous aluminum chloride was placed in the flask and covered with 100 cc. of anhydrous benzene. The mixture was brought to refluxing temperature over a steam bath with vigorous stirring. Only a part of the aluminum chloride dissolved in the benzene and the solution acquired a light yellow-brown color. Hydrogen chloride was evolved quite rapidly as the benzene began to boil. This was believed to be due to the formation of a benzene-aluminum chloride addition product rather than hydrolysis of the anhydrous salt since the benzene had been kept over sodium and contained no moisture. Through the addition funnel 10.7 cc. (.13 mols, 12.3 g.) of chloroacetone was allowed to drop slowly into the vigorously stirred reaction mixture. As each drop of chloroacetone hit the surface of the hot solution, hydrogen

chloride was evolved violently. The rate of addition of the reagent was governed by the rate of evolution of the gas; usually about thirty minutes were required for adding the 10.7 cc. used. At this point the reaction mixture had acquired a bright red color. Refluxing was continued for four hours and the mixture was stirred throughout the entire period. As the reaction proceeded, color became progressively darker until at the end of the refluxing period the mixture appeared practically black. For the first two hours after all the chloroacetone had been added, hydrogen chloride was evolved continuously though not violently. The rate of evolution, however, gradually decreased until, after three to three and one-half hours of refluxing, virtually no fumes were being evolved, and the water from the gas absorption bottle had no effect on litmus paper.

At the end of the reflux period, cold water was circulated in the steam bath. When the contents of the flask were cooled to room temperature, the product was decomposed by allowing water to drop in through the addition funnel. This technic of decomposition is in marked contrast to that usually recommended for Friedel-Crafts addition products of aluminum chloride; the usual procedure being to pour the contents of the flask over cracked ice. The method used here was a great deal more convenient, and although the decomposition reaction was exothermic,

the addition of the water could easily be accomplished without the contents of the flask boiling. Approximately the first 25 cc. of water added brought about the violent evolution of hydrogen chloride, and the rate of addition was governed by the rate of evolution of the gas. When no more hydrogen chloride was evolved, 20 cc. excess water was run in and 20 cc. of concentrated hydrochloric acid was added to dissolve any basic aluminum chloride present. At this point the flask contained two layers; the top layer consisted of about 100 cc. of dark brown benzene solution of the oil and the bottom layer about 175 cc. of aqueous aluminum chloride solution. The aqueous layer was only slightly colored. Two different methods of working up the product were used in the various runs. They will be referred to later as procedure A or B for working up the product.

Procedure A involved the removal of the benzene by steam distillation. The remaining oil was separated from the aqueous layer and the latter extracted with one or two portions of ether. The aqueous layer was practically clear and colorless after this treatment, indicating that the ether had removed all the organic oil. The benzene layer of the steam distillate was distilled to remove the benzene and water; any remaining yellow oil was combined with the ethereal solution. The ether was

removed from the solution over a steam bath and the remaining oil transferred to a 50 cc. Claissen flask.

Procedure B consisted of a benzene extraction of the oil. The steam distillation was omitted and the use of ether was avoided. The benzene layer was first separated from the aqueous layer; then the latter was extracted with four 25 cc. portions of benzene using a large separatory funnel. The last extraction was colored only very slightly. The extractions were combined with the benzene layer and the solution was run through a rapid filter which retained droplets of water and any solid particles present. The benzene was distilled from the solution using a 500 cc. bolt-head flask and a two-bulb fractionating column filled with short pieces of glass tubing. The remaining viscous oil was transferred to a 50 cc. Claissen flask. A 10 cc. portion of benzene was used to rinse the large flask and was added to the oil. All the benzene was removed from the oil by heating to a temperature of 90°C . at atmospheric pressure.

It was thought that procedure B would be better for several reasons. In the steam distillation of procedure A, part of the phenylacetone distilled over with the benzene, making it necessary to recover the phenylacetone from both the distillate and the residue. The extraction with benzene (procedure B) would be a satisfactory method of separating the oil from the aqueous layer. Another point in favor of procedure B was that in distilling the benzene from the solu-

tion, a water-benzene mixture would distill over until all moisture was removed. This would afford an excellent method of drying the product before the vacuum distillation.

The dark viscous oil was distilled under a pressure of 20-22 mm. The volume of the oil was usually between 25 and 35 cc, and considerable difficulty due to superheating and bumping was encountered. The use of a capillary and allowing air to bubble through the oil did not prevent the bumping, nor did the use of ebullition tubes or glass beads help. It was found that by very careful heating near the surface with a ring burner, the distillation could be carried out successfully. In general the following fractions of distillate were collected: A, boiling below 110°C; B, boiling at 110°-123°C; C, boiling at 123°-180°C; and D, the residue. The amount of fraction B was considered as a measure of the relative yield of phenylacetone in the runs that follow. Phenylacetone boils at 110°-115°C under a pressure of 20-22 mm(18). In certain runs an additional high-boiling fraction was collected above fraction C. In general fraction A was practically colorless, fraction B possessed a light yellow color, fraction C was light red or brown, and the higher fractions were progressively darker.

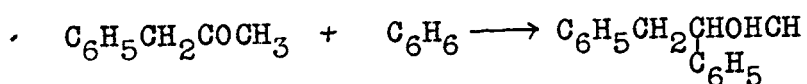
Run One

The decision to add the chloroacetone to the hot benzene and aluminum chloride was based upon a run made by Chamberlin(1) using aluminum chloride and chloroacetone in an inert solvent. He found that when 10.7 cc. of chloroacetone, 34 g. of aluminum chloride, and 100 cc. of symmetrical tetra-chloro-ethane were heated on a steam bath for six hours, only about thirty percent of the chloroacetone was recoverable. The remainder formed black tarry material which was not identified. The conclusion that chloroacetone underwent some form of polymerization was borne out in another run in which chloroacetone was in excess and acted as the solvent; the reaction mixture became black, tarry and quite viscous so that stirring was almost impossible.

In the run that follows, it was expected that more phenylacetone would be formed if the chloroacetone were added slowly and in such a fashion that it reacted with the benzene before its concentration became great enough for appreciable polymerization to take place. The general procedure was followed throughout. Procedure A for working up the reaction mixture was used; 8 g. of product was obtained in fraction B (110° - 123° C) and 7 g. in fraction C (123° - 180° C).

Run Two

A review of side reactions commonly taking place in Friedel-Crafts preparations(19) indicated that if phenylacetone were formed, its aluminum chloride addition compound might react with another molecule of benzene to form methyl phenyl benzyl carbinol, thus:



To test this possibility 23.1 g. (.25 mols) of chloroacetone, 70 g. (.52 mols) aluminum chloride and 150 cc. of benzene were used. Thus, while the quantities of chloroacetone and aluminum chloride were doubled, that of benzene was increased only enough to give a mobile mixture; i.e., fifty percent. It was expected that if the above side reaction took place this change in the ratio of reactants would decrease its magnitude and increase the quantity of phenylacetone obtained. The general procedure for preparation was followed without exception. Procedure A was used for working up the mixture and the yield of fraction B was 8.5 g. Hence no increase in phenylacetone yield was observed; furthermore, as is discussed in another paragraph, the high-boiling fraction showed no reactions of an alcohol.

(19) Calloway, Chem. Rev. 17, 327 (1935)

Run Three

To test the possibility that polymerization of the chloroacetone took place only at a higher temperature than its reaction with benzene, this preparation was attempted at a temperature lower than that of boiling benzene. A thermometer was placed in the reaction mixture. The general procedure was followed with the exceptions noted below. It was intended that the temperature should not be greater than that necessary for reaction to take place. The chloroacetone was run in at room temperature over a period of ten minutes. There was no evolution of heat nor was appreciable hydrogen chloride evolved. Stirring the mixture for ninety minutes failed to bring about any reaction as evidenced by the neutrality to litmus of the water from the gas absorption bottle. During this period, however, the solution became bright red probably indicating that the aluminum chloride addition product of chloroacetone was being formed. The temperature of the reaction mixture was raised to 40°C. for two hours; there was very little hydrogen chloride evolved. Stirring was discontinued and the mixture stood at room temperature for ten hours. Stirring was resumed and the temperature brought to 50°C. for three hours. The amount of hydrogen chloride evolved was small. At 60°C. it was given off somewhat more rapidly for a few minutes. Then, at 70°C. for ten minutes, no

hydrogen chloride was given off and the reaction was discontinued. Procedure B was used to work up the reaction mixture. Distillation at atmospheric pressure was effected; the yield of phenylacetone was less than three grams.

Run Four

A small amount of copper powder was added as an auxiliary catalyst. The amounts of reactants and the conditions of the general procedure for preparation were used with the exceptions noted below. With the aluminum chloride 2 g. of copper powder was introduced into the reaction mixture. The copper powder was coated with copper oxide; it was used without being reduced. The chloroacetone was added at room temperature and the temperature gradually increased. At approximately 55°C. hydrogen chloride evolution began. The temperature was brought to 80°C. for five and one-half hours. Procedure B for working up the product was used. Distillation of the oil at atmospheric pressure failed to give any sharp fraction in the vicinity of 216°C., the boiling point of phenylacetone. The following fractions were, however, collected: 5 g. boiling at 90°-210°C.; 5 g. boiling at 210°-260°C.; 3 g. boiling at 260°-320°C.; and several grams of black semi-solid tar.

Run Five

Copper powder only was used as a catalyst. Crook and Davies(20) found that by refluxing ethyl bromo-acetate and thionaphthene for a long period of time, thionaphthene-acetic acid and a thionaphthene-di-acetic acid was produced. If copper powder were added from time to time during the heating, the amount of the thionaphthene-di-acetic acid was reduced considerably. In a Friedel-Crafts reaction there is always the possibility of condensing two or more aliphatic chains to one aromatic molecule. If copper could be made to effect the condensation of benzene and chloroacetone at all, it was expected that its presence would reduce, therefore, the formation of phenylene-diacetone.

The amounts of reagents stated in the general procedure were used with the exception that aluminum chloride was omitted. At the beginning 0.5 g. copper powder (copper oxide coated) was introduced with the benzene and chloroacetone. A total of 35 g. was finally added in small portions at irregular intervals. The total time of refluxing was sixty hours and the reaction was interrupted five times and allowed to stand over-night at room temperature. The reaction mixture was filtered to remove the copper powder and a large part of the benzene was removed using the two-

(20) J. Chem. Soc. Lond., p 1697 (1935)

bulb fractionating column. Practically all of the product distilled at less than 150°C . and it was concluded from its odor and lachrymatory properties to contain chloroacetone. No phenylacetone was formed.

Runs Six, Seven, Eight, and Nine

The time of reaction factor was next investigated. It has been pointed out by Calloway(19) that in general for Friedel-Crafts reactions, the fact that hydrogen chloride evolution has ceased, is not sufficient evidence that reaction is complete. If phenylacetone were formed in a relatively short time in this reaction and then, during the four hours of heating, entered into some reaction forming another product, the reduction of time of reaction would be expected to increase the phenylacetone obtained. On the other hand if the process of activation of the reacting molecules takes place slowly, an increase in the amount of time allowed for reaction would bring the condensation of the activated molecules nearer to completion.

In the following runs, time of refluxing was the only variation in conditions; otherwise, the general procedure was followed carefully. Procedure B for working up the reaction product was followed.

In run six, following the addition of the chloroacetone, the reaction was discontinued after one hour of refluxing. The reaction product was not as dark colored nor as viscous as that obtained in previous runs. Four grams of phenylacetone was obtained; the yield of the higher fractions was considerably less than when the reaction was allowed to

(19) Calloway, Chem. Rev. 17, 327 (1935)

proceed for four hours.

The reaction was allowed to proceed two hours in run seven. There was hydrogen chloride being evolved at the time refluxing was discontinued; the rate was estimated at a bubble every two seconds. The yield of fraction B (110° - 123° C./20-22mm) was 3.5 g. and there was considerable high-boiling fraction.

In run eight the reaction was allowed to proceed three hours after the addition of chloroacetone. Before it was decomposed with water, the product stood at room temperature for three more hours. The distillation yielded 4 g. of fraction A (less than 110° C./20-22 mm), 4 g. of fraction B (110° - 123° C./20-22 mm), and 2 g. of fraction C (123° - 180° C./20-22 mm).

Run nine was refluxed for five hours. After the first half hour of refluxing, the mixture had acquired a golden yellow color. It became progressively darker until at the end of the refluxing period it appeared black. Practically no hydrogen chloride was being evolved. The vacuum distillation gave 3.5 g. of fraction A (less than 110° C./20-22 mm), 5 g. of fraction B (110° - 123° C./20-22 mm), 3 g. of fraction C (123° - 180° C./20-22 mm), and about 7 g. of residue. Fraction A was pale yellow, fraction B almost colorless, fraction C reddish brown, and the residue was black and viscous.

Run Ten

It was found that the phenylacetone in previous runs readily formed a sodium bisulfite addition product. If this addition product could be formed in the benzene solution of the reaction product, its hydrolysis would afford an excellent means of obtaining the phenylacetone in a relatively pure condition. Accordingly, a run was made following the general procedure for preparation; the reaction product was extracted with benzene as in procedure B.

The sodium bisulfite reagent was made by shaking a 5-1 ratio of 40% sodium bisulfite water solution and alcohol and filtering the excess sodium bisulfite. Fifty cubic centimeters of this reagent was added to the benzene solution. The mixture was placed in the original reaction flask and brought to reflux temperature over a steam bath. It was heated thus for ten minutes with vigorous stirring. After standing over-night at room temperature, there was no evidence of the formation of an addition product. A small amount of white solid at the bottom of the flask failed to give any carbonyl oil upon treatment with sodium carbonate solution. It was concluded, therefore, that the bisulfite addition product of phenylacetone could not be formed in this manner.

Run Eleven

The usual procedure for introducing an aliphatic chain into an aromatic nucleus by means of condensation with aluminum chloride provides for the addition of the aluminum chloride in small portions to the reactants at room temperature.

Through a second condenser the aluminum chloride was added in seven portions to refluxing chloroacetone and benzene over a period of two hours after which refluxing was continued for three hours. All other details of the general procedure for preparation and procedure B for working up the reaction product were followed. The distillation yielded 2 g. of fraction A (less than $110^{\circ}\text{C.}/20\text{-}22\text{ mm}$), 3 g. of fraction B ($110^{\circ}\text{-}123^{\circ}\text{C.}/20\text{-}22\text{ mm}$), and 2 g. of fraction C ($123^{\circ}\text{-}180^{\circ}\text{C.}/20\text{-}22\text{ mm}$). Thus there was no improvement in the yield of phenylacetone.

Run Twelve

In several previous runs it had been observed that the evolution of hydrogen chloride decreased in violence as the last three or four cubic centimeters of chloroacetone dropped into the hot benzene and aluminum chloride. Near the first of the addition each drop had provoked a violent evolution of hydrogen chloride.

To test the possibility that an insufficient amount of aluminum chloride was being used to give the reaction optimum speed, the ratio of aluminum chloride to chloroacetone was increased to 2.5 to 1. Instead of the usual 34 g., 43.5 (.32 mols) of aluminum chloride was used with the usual 10.7 cc. (.13 mols, 12.3 g.) of chloroacetone and 100 cc. of benzene. The general procedure was followed and copious evolution of hydrogen chloride continued with each drop until all chloroacetone was added. Procedure A for working up the product was carried out and distillation gave 5 g. of fraction A (less than 110° C./20-22 mm) and 4 g. of fraction B (110°-123° C./20-22 mm). No improvement in the yield of phenylacetone was effected by the increase of aluminum chloride used.

Run Thirteen

If a larger percentage of phenylacetone was being formed than was being obtained in the final distillation, an increase in the amount of materials used would give a greater relative yield in the end. Thus, to test the efficiency of the method of purification, the quantity of all reactants was tripled. The general procedure for preparation and modification B for purification was followed. The distillation gave 4 g. of fraction A (less than 110° C./20-22 mm), 15 g. of fraction B (110°-123° C./20-22mm), and 5 g. of fraction C (123°-180° C./20-22 mm). The run gave no greater relative yield of fraction B, but it did give a sharper fraction.

Runs Fourteen and Fifteen

In order to compare the methods A and B for working up the reaction product, these two runs were made. The amounts of reactants and the conditions of general procedure for preparation were used in both cases. The yield using procedure A was; fraction A (less than 110°C/20-22 mm), 4.5 g.; fraction B (110°-123° C./20-22 mm), 4 g.; and fraction C (123°-180° C./20-22 mm), 3 g. The yield using procedure B was; fraction A, 5.5 g.; fraction B, 5 g. and fraction C, 4 g. It was concluded that procedure B for working up the product was more efficient than procedure A.

Run Sixteen

It had been admittedly difficult to draw definite conclusions concerning the yield of phenylacetone from many of the preceding runs. Although much helpful information was obtained, it was thought that poor and varying separation of the phenylacetone from benzene and from the high-boiling fraction had made yields in many cases almost meaningless. This run was undertaken with the hope of effecting a better separation of phenylacetone from the high-boiling material. It was thought that the phenylacetone might be more volatile with steam than the high-boiling material. The general procedure was followed. The benzene was removed by steam distillation as in procedure A. The course of the steam distillation was followed by removing samples of the distillate and testing with sodium bisulfite solution. The test was made by allowing the oil to stand in contact with the bisulfite reagent for one-half hour. It was found that the higher boiling oil distilled with steam, for samples of the distillate failed to give a bisulfite reaction. This indicated that this method of separation was no better than previous methods.

Run Seventeen

This run was made under the optimum conditions as determined in all the foregoing runs. In order to determine the exact percentage of pure phenylacetone that the preparation would give, the purification was carried through the sodium bisulfite addition product and its hydrolysis as described in detail in the "Purification and Identification" part of this paper.

The amounts of materials and the details of procedure of the general procedure described at the beginning of the "Experimental Part" were used with exceptions noted below. It might be said that the general procedure was not the method used at the outset of this investigation, but it was written, after the major part of the work was complete, to make it possible to describe the individual runs and modifications of conditions with economy of time and space. It necessarily includes certain of the improvements adopted.

The refluxing was continued for five hours after the addition of chloroacetone was complete. At this time practically no hydrogen chloride was being evolved. Procedure B for working up the reaction mixture was used, and the benzene was removed by distillation up to 100°C. at atmospheric pressure. The vacuum distillation yielded 8 g. of fraction A and B boiling at less than 123°C./20-22 mm.

The fractions A and B were collected together. Of fraction C (123°-180°C./20-22 mm) there was 2.5 g., and there was about 7 g. of tarry residue.

From the 8 g. of fraction A and B, 21.5 g. of sodium bisulfite addition product was prepared. This was a yield of 149% and meant only that the addition product contained uncombined sodium bisulfite. From the fraction C 0.5 g. of addition product was obtained. To the 21.7 g. of addition product in a 200 cc. bolt-head flask 12 g. of sodium carbonate and 75 cc. of water was added and the mixture steam distilled until no more oil came over in the distillate. The distillate was then extracted with three 10 cc. portions of ether and the ether solution dried over anhydrous magnesium sulfate for twenty-four hours. The magnesium sulfate was filtered out and was washed with one 10 cc. portion of anhydrous ether. The ether was removed from the phenylacetone by distillation over a steam bath and the warm phenylacetone was placed in a vacuum desiccator for two hours. The yield of phenylacetone obtained was 7.5 g. which represented 61% of the theoretical calculated from the addition product hydrolyzed. The low percentage of recovery was further evidence that the addition product was contaminated. The yield of phenylacetone calculated on the basis of the 12.3 g. of chloroacetone used was 41% of the theoretical.

PURIFICATION AND IDENTIFICATION

The fraction B, run three, was subjected to a temperature of -50°C . and failed to solidify. The melting point of phenylacetone is -15.4°C . The index of refraction of the same product was $N_D^{20} 1.523$ while that of phenylacetone is $N_D^{20} 1.5169$. Thus it was evident that this phenylacetone contained water, traces of solvent, or some other impurity. Definitely, further purification would be necessary before positive identification of phenylacetone could be made.

Accordingly, using the fraction B from runs one and two, 10 g. of the bisulfite addition product was prepared according to the instructions of Shriner and Fuson(21). After shaking, the whole contents of the test tube became a semi-solid pasty mass. On a suction filter as much as possible of the mother liquor was pressed out and the white solid was placed on a filter paper to dry. The bisulfite addition product was hydrolyzed by adding 5 g. of sodium carbonate and 75 cc. of water. After warming for one-half hour, the carbonyl oil that had separated out on top of the aqueous layer was extracted with ether. The ether was removed by distillation over a steam bath. The micro-boiling point of this product was 220.5°C . (corrected). This was above that of phenylacetone; namely, 216°C . The index of

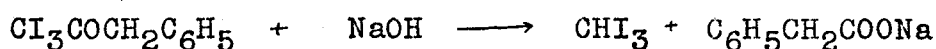
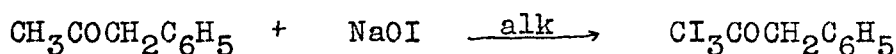
(21) Shriner and Fuson, Identification of Organic Compounds

p. 32 (1935)

refraction of this product was N_D^{20} 1.519. This is nearer to the literature figure than that of the original fraction B; however, even this figure is too much at variance with N_D^{20} 1.5169 to be accepted as positive identification of phenylacetone. It is probable that the sample underwent some decomposition when the micro-boiling point was taken.

Phenylacetone was expected to yield iodoform when treated with an alkaline solution of iodine in potassium iodide.

The reactions



are general for compounds of the formula CH_3COR . Indeed, Heilbron(22) reported that phenylacetone gave the iodoform reaction.

One-half cubic centimeter of fraction B was dissolved in 10 cc. of dioxane. One cubic centimeter of 10% sodium hydroxide solution was added. Iodine in potassium iodide was added in small quantities until the color of iodine remained after three minutes heating at 60°C . The excess dark color was removed with a few drops of alkali and the mixture was diluted to three times its volume with water. This gave an orange-yellow suspension which showed globules of oil after standing for several days. Acetone treated

(22) Heilbron, Dict. Org. Compds. II, 633 (1936)

in the same way at the same time gave a precipitate of iodoform below a clear solution.

The test was tried without dioxane as a solvent, but no iodoform was obtained.

The fraction B from runs ten, twelve, and thirteen were combined and redistilled under reduced pressure. The fraction boiling at 110° - 115° C./20-22 mm was collected. One gram was treated with alkaline sodium hypiodite solution as above using dioxane as a solvent. The solution was refluxed for twelve hours, but upon dilution no iodoform was obtained.

It was reported that phenylacetone reacted with calcium hypochlorite, $\text{Ca}(\text{OCl})_2$ solution yielding benzaldehyde, benzoic acid, and acetic acid(23). In order to determine whether the iodination was taking place on the methylene group rather than the methyl group in the foregoing iodoform tests, an attempt was made to isolate benzoic acid from the reaction mixture of an iodoform test. To assure complete oxidation to acids, the temperature of the iodination was raised to 100 C. To facilitate isolation of the benzoic acid, only water was used as a solvent.

To 1 g. of phenylacetone, obtained from the hydrolysis of the bisulfite addition product, was added 10 cc. of iodine in potassium iodide solution, 1 cc. of 10% sodium hydroxide solution, and 10 cc. of water. The mixture was

(23) Suknevich and Chilingaryan, C. A. 30, 5937⁴ (1936)

refluxed for twelve hours and as the solution became lighter in color, 12 cc. more of iodine-potassium iodide solution was added at intervals. The alkaline reaction mixture was extracted with several small portions of ether and the aqueous solution was acidified with sulfuric acid. No benzoic acid precipitated even after the solution was seeded with a small crystal of it.

Tests with phenylhydrazine made on another sample of phenylacetone after the same treatment with potassium hypoiodite, failed to show the presence of a carbonyl compound. Further tests with larger quantities of material will have to be made before the course of the iodination can be determined.

Two attempts to prepare the oxime from a fraction B according to instructions of Shriner and Fuson(24) failed to yield any crystalline product. The melting point of the oxime of phenylacetone is reported in the literature at 63°C.

The preparation of the phenylhydrazone from a fraction B according to instructions of Shriner and Fuson(25) gave a liquid which crystallized in the solution after standing over-night. Purification by recrystallization from alcohol was effected, but the white crystals seemed quite unstable and became colored brown on standing in air for a few minutes.

(24) Shriner and Fuson, Ident. Org. Compds. p 145 (1935)

(25) *ibid*, p 37

Its melting point was not sharp, 74° - 77° C., eight degrees below the literature melting point of 84° C.

The semicarbazone of fraction B, run three, was prepared and recrystallized from an alcohol-water solution. It was dried in air for an hour and melted at 178° - 180° C. It was again recrystallized from 95% alcohol and dried in a desiccator over sulfuric acid for forty-eight hours. It melted 182° - 184° C. There are several melting points of the semicarbazone of phenylacetone reported in the chemical literature; 184° , 188° , and 197° C. being reported by various workers.

Twenty-three grams of the sodium bisulfite addition product was prepared. To it, 10 g. of sodium carbonate and 75 cc. of water was added and the mixture warmed for twenty minutes. A clear, almost colorless oil appeared on top. The mixture was steam distilled yielding globules of practically colorless oil dispersed in the water. The oil was extracted with several portions of ether and dried over anhydrous calcium chloride. The color of the ether solution became yellow during the process of drying. This may have been due to the formation of a compound between calcium chloride and phenylacetone. Ether was distilled from the decanted ether solution leaving 8 g. of brown liquid representing a yield of 61% calculated on the basis of the weight of bisulfite addition product used. Due to the color this was set aside and no tests were made on it.

Sixteen and one-half grams of sodium bisulfite addition product was prepared, hydrolyzed with sodium carbonate solution, and steam distilled. Two cubic centimeters of the oil was removed from the steam distillate with a pipette; it was warmed in a small test tube and placed in a vacuum desiccator over sulfuric acid over-night. Its index of refraction was n_D^{20} 1.518. The remainder of the oil was extracted from the steam distillate with ether and dried over magnesium sulfate for twenty-four hours. The drying agent was removed by filtration, the ether by distillation, and the remaining oil was placed in the vacuum desiccator over-night. There was 3.5 cc. of it which with the 2 cc. removed above represented a yield of 59 % from the bisulfite addition product. Its index of refraction was determined, n_D^{20} 1.518.

This product was cooled to -35°C . and scratching the walls of the test tube caused it to solidify. Upon gradual warming a melting point of -12°C was obtained.

The semicarbazone of this sample was prepared and recrystallized from 50% alcohol and dried for thirty-six hours in a vacuum desiccator; melting point $180^{\circ}\text{--}185^{\circ}\text{C}$. Recrystallization from absolute alcohol and vacuum drying raised the melting point to $191^{\circ}\text{--}192^{\circ}\text{C}$.

From 15.5 g. of phenylacetone obtained from bisulfite addition product hydrolysis was used to prepare the semicarbazone. A yield of 22 g. was obtained which represented

100% calculated from the amount of phenylacetone used. It was in all probability contaminated with sodium acetate which was added in the preparation to hydrolyze the semicarbazide hydrochloride. It was recrystallized twice from 50% alcohol and dried in a vacuum desiccator over-night. It melted 184° - 188° C. The same sample was recrystallized twice more from absolute alcohol and after drying over-night in a vacuum desiccator melted at 188° - 189° C. Further recrystallizations gave no increase in the melting point.

A sample of the semicarbazone was dried in an oven at 110° C. and a Kjeldahl nitrogen determination made. The results were low, 13% nitrogen as compared to 22% nitrogen calculated for the compound. This large discrepancy could not be explained by impurities; therefore, was thought to be due to incomplete conversion of the nitrogen to ammonia.

Another sample was reduced with tin and hydrochloric acid before the Kjeldahl digestion. The 17% nitrogen obtained was better than before, but it indicated that conversion to ammonia was still incomplete. Evidently more drastic reduction is necessary to convert the nitrogen of semicarbazones than of other types of organic compounds.

From 27 g. of crude phenylacetone (fractions A and B) 56.5 g. of bisulfite addition product was prepared. It was washed once with alcohol and once with ether to remove any non-carbonyl oil. To the addition product placed in a 500 cc. bolt-head flask, 12 g. sodium carbonate and 150 cc.

of water was added and the phenylacetone removed by steam distillation. The phenylacetone was extracted from the steam distillate with three portions of ether. The ether solution was dried over anhydrous magnesium sulfate for twenty-four hours. The drying agent was removed by filtering and the solvent was removed by evaporation. After drying in the vacuum desiccator the phenylacetone obtained had a blue fluorescence. The 21 g. yield represented 60% from the addition product used. This yield and that of phenylacetone from other hydrolyses of the bisulfite addition product appears at first to be very poor recovery. However, it must be noted that the yields of bisulfite addition product calculated from the weights of crude phenylacetone used was well over 100%. It was concluded that every sample of the bisulfite addition product produced contained considerable uncombined sodium bisulfite.

Three carbon-hydrogen determinations were made on samples of the 21 g. of phenylacetone obtained above. The results:

	Carbon	Hydrogen	Carbon/Hydrogen ratio
Theoretical	80.57%	7.51%	10.73
# 1	79.39%	7.45%	10.61
# 2	80.49%	7.59%	10.65
# 3	79.89%	7.55%	10.58
Mean	79.92%	7.53%	

Its index of refraction was n_D^{20} 1.5175 and its density was

1.005 $20^{\circ}/4^{\circ}$. These may be compared with the reported index of refraction of N_D^{20} 1.5169 and the International Critical Tables density of 1.028 $20^{\circ}/4^{\circ}$.

Twenty grams of the pure phenylacetone was redistilled under a pressure of 20-22 mm. It distilled at a relatively constant temperature near 110°C . The density of this distillate was 1.005 $20^{\circ}/4^{\circ}$ and its index of refraction N_D^{20} 1.5169. Its melting point of -15.3°C . compared favorably with that of -15.4°C . reported in the International Critical Tables.

NATURE OF BY-PRODUCTS

Obviously, any information as to the nature of the products of side reactions and their method of formation would be helpful. Modifications in the conditions of preparation could be made tending to decrease the rate of these side reactions and favor the formation of the phenylacetone. With this object in view, tests were made on various fractions.

If phenylene diacetone were present in the reaction products, it should give reactions peculiar to a carbonyl compound. Fraction C of run one failed to give a sodium bisulfite addition product even upon standing over-night. The oil remained above the bisulfite reagent. Treatment with sodium hypiodite failed to yield any iodoform.

For further tests the fractions C and D remaining from runs one through nine were combined in benzene solution and redistilled under reduced pressure. The following fractions were collected: boiling at less than $120^{\circ}\text{C.}/10\text{-}12\text{ mm}$, 4 g.; boiling at $120^{\circ}\text{-}160^{\circ}\text{C.}/10\text{-}12\text{ mm}$, 8 g.; boiling at $160^{\circ}\text{-}200^{\circ}\text{C.}/10\text{ mm}$, 10 g.; boiling at $200^{\circ}\text{-}260^{\circ}\text{C.}/10\text{ mm}$, 11 g.; boiling at $260^{\circ}\text{-}320^{\circ}\text{C.}/10\text{ mm}$, 4 g.; and approximately 15 g. of residue.

If methyl benzyl phenyl carbinol were formed as proposed in the discussion of run two, it would be found in the high-boiling fraction, boiling point $175^{\circ}\text{C.}/15\text{ mm}$. It should cause this fraction to give reactions characteristic of

alcohols. The several fractions of high-boiling oil did not react with metallic sodium nor with acetyl chloride. An attempt to prepare the phenyl-urethan failed to give a derivative. It was therefore concluded that the high-boiling liquid contained no alcohol.

SUMMARY

Phenylacetone has been prepared from benzene and chloroacetone in the presence of aluminum chloride with a yield of 41% calculated on the basis of the chloroacetone used. Seventeen runs were made in order to determine the optimum conditions for the reaction and the most efficient method of purification. The method of bringing the reactants together, the temperature of the reaction, the ratio of the reactants, and the time of reaction were factors investigated. The following procedure is thought to be optimum.

A 500 cc. three-neck flask is provided with a mercury seal stirrer, a water condenser, and a small addition funnel. The condenser is connected to a double trap of concentrated sulfuric acid, and a gas absorption bottle is connected to the trap.

Thirty-four grams of anhydrous aluminum chloride is placed in the flask and covered with 100 cc. of anhydrous benzene. The mixture is brought to refluxing temperature over a steam bath with vigorous stirring. Through the addition funnel 10.7 cc. of chloroacetone is allowed to drop in slowly. Refluxing is continued for five hours and the mixture is stirred throughout the heating period.

At the end of the reflux period, cold water is circulated in the steam bath. When the contents of the flask cool to room temperature, the product is decomposed by

allowing water to drop in through the addition funnel. When no more hydrogen chloride evolves, 20 cc. excess water is run in and 20 cc. concentrated hydrochloric acid is added.

The benzene layer is separated from the aqueous layer and the latter extracted with four 25 cc. portions of benzene. The extractions are combined with the benzene layer and the solution run through a rapid filter. The benzene is distilled from the solution by heating to a temperature of 90°C . using a 500 cc. bolt-head flask and a two-bulb fractionating column filled with glass tubing.

The viscous oily residue is transferred to a 50 cc. Claissen flask; a 10 cc. portion of benzene is used to rinse the large flask and added to the oil. The remaining benzene is removed at atmospheric pressure, and the oil distilled under a pressure of 20-22 mm. The fraction boiling at less than 130°C . contains practically all of the phenylacetone. To this fraction in a 250 cc. beaker is added five times its volume of sodium bisulfite reagent. It is allowed to stand for at least thirty minutes with occasional stirring. On a suction filter the mother liquor is removed and the addition product washed with one 5 cc. portion of alcohol followed by a 5 cc. portion of ether. The dry bisulfite addition product is placed in a 200 cc. bolt-head flask and hydrolyzed by adding 12 g. of sodium carbonate and 75 cc. water. The mixture is steam distilled until no more oil is volatilized with the steam. The distillate is extracted

with three 10 cc. portions of ether and the ether solution of phenylacetone dried over magnesium sulfate. The magnesium sulfate is removed by filtering and the ether is distilled over a steam bath. Last traces of solvent are removed from the phenylacetone by placing it while warm in a vacuum desiccator and allowing it to stand for two hours.

Above 90% of the crude phenylacetone obtained in the vacuum distillation was usually recovered from the bisulfite addition product hydrolysis as pure phenylacetone. The fact that more than 100% yields of bisulfite addition product was obtained showed that it contained considerable uncombined sodium bisulfite.

The pure phenylacetone had a density of 1.005 $20^{\circ}/4^{\circ}$ and an index of refraction of N_D^{20} 1.5175. A redistilled sample of this gave an index of refraction of N_D^{20} 1.5169 and melted at -15.3°C . The literature recording of these constants are N_D^{20} 1.5169, d_4^{20} 1.028, and melting point -15.4°C .

Attempts to prepare and purify the phenylhydrazone and the oxime of phenylacetone were unsuccessful. The purest semicarbazone obtained melted at $188^{\circ}\text{--}189^{\circ}\text{C}$. Kjeldahl nitrogen determinations on the semicarbazone were low (17% compared to 22% theoretical) even after the sample was previously reduced.

No compound was identified in the high-boiling fraction. It was found to give no reactions of an alcohol nor a carbonyl group.

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