The mercury analyses were carried out according to Rauscher's method as modified by us.[4]

Summary

Several series of aromatic glycol mercurials have been prepared and their bactericidal properties evaluated. An attempt has been made to correlate the antibacterial activity with the structure of the mercurials.

NEW YORK, N. Y. RECEIVED JUNE 1, 1944

(4) Shukis and Tallman, *Ind. Eng. Chem.*, *Anal. Ed.*, **12**, 123 (1940).

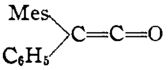
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

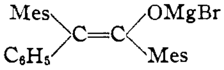
Vinyl Alcohols. XIII.[1] 1,2-Dimesityl-2-phenylvinyl Alcohol

BY REYNOLD C. FUSON, L. J. ARMSTRONG,[2] J. WAYNE KNEISLEY[3] AND W. J. SHENK, JR.

The condensation of diphenylketene[4] and of mesitylketene[5] with Grignard reagents has been shown to yield unstable vinyl alcohols. By proper choice of substituents it appeared possible to synthesize in this way vinyl alcohols which would be stable. This paper reports such a synthesis.

When mesitylphenylketene (I) was treated with mesitylmagnesium bromide the enolate (II) of 1,2-dimesityl-2-phenylvinyl alcohol (III) was formed. Treatment of the reaction mixture with acetyl chloride produced an acetate (m. p. 179.5–180.5°) and with dilute acids the free vinyl alcohol (m. p. 139–140°). A second acetate (m. p. 160–161°), evidently the *cis–trans* isomer of the first, was obtained by treatment of the alcohol with acetic anhydride in the presence of pyridine. Since both acetates yielded the same alcohol when hydrolyzed, it appears that in one of these reactions a change of configuration must have occurred. A similar observation was made by Kohler and Thompson,[6] who obtained the same enol peroxide from the *cis* and *trans* enolates of benzohydrylacetomesitylene. The vinyl alcohol is clearly one of the two possible *cis–trans* isomers corresponding to the two acetates. The other has not yet been found.


I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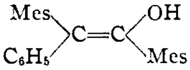
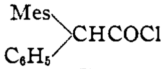
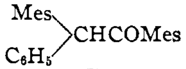

III

Perhaps the most significant observation in this connection was that the product obtained from mesitylphenylacetyl chloride (IV) and mesitylmagnesium bromide was not a vinyl alcohol at all but the corresponding ketone, α-phenyldesoxymesitoin (V). Its properties contrast sharply with those of the enol. Infrared spectra[7] showed absorption maxima at 2.86 and 2.78 μ, confirming the presence of a hydroxyl group in the enol. A maximum at 5.88 μ was observed in the spectrum of the ketone, showing the presence of a carbonyl group.


IV


V

The ketone, as would be expected, failed to yield an acetate. Under the influence of sodium ethoxide, however, it was isomerized to the enol (III). The production of the ketone in this manner can be explained on the assumption that the Grignard reagent does not add to the carbonyl group of the acid chloride but merely replaces the chloride atom by direct metathesis. The structure of the ketone was confirmed by its synthesis from α-chlorophenacetyl chloride and mesitylene by the Friedel–Crafts method.

Mesitylphenylketene (I) was made first from mesityl phenyl diketone by the general method of Schroeter[8] as modified by Smith and Hoehn.[9] A far better method, however, was developed by which the ketene could be made from mandelic acid and mesitylene. The conversion of mandelic acid to mesitylphenylacetic acid was effected in 61% yield according to a procedure similar to that used by Gyr[10] to prepare phenyl-*p*-tolylacetic acid. The acid chloride, produced by a method developed by Fieser and Fieser,[11] was dehydrochlorinated by heating with pyridine. The yield of ketene, based on the acid, was 78%.

Experimental

Mesityl Phenyl Diketone Monohydrazone.—Twenty cubic centimeters of 85% hydrazine hydrate solution was dropped into a hot solution of 40 g. of mesityl phenyl diketone in 1 liter of methanol. The reaction mixture was heated under reflux for thirty hours and cooled to 0°. The hydrazone, which separated in the form of white needles, was recrystallized from methanol; m. p. 186–188°; yield 5 g.

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(1) For the preceding paper of this series see Fuson, Armstrong, Wallace and Kneisley, THIS JOURNAL, **66**, 1274 (1944).

(2) Present address: Rohm and Haas Company, Philadelphia, Pennsylvania.

(3) Present address: Hercules Powder Company, Wilmington, Delaware.

(4) Gilman and Heckert, THIS JOURNAL, **42**, 1010 (1920).

(5) Fuson, Armstrong and Shenk, *ibid.*, **66**, 964 (1944).

(6) Kohler and Thompson, *ibid.*, **59**, 887 (1937).

(7) The authors are indebted to Professor W. H. Rodebush and Mr. Robert Whitney for the measurement and interpretation of the absorption spectra mentioned in this paper.

(8) Schroeter, *Ber.*, **42**, 2346 (1909).

(9) Smith and Hoehn, "Organic Syntheses," **20**, 47 (1940).

(10) Gyr, *Ber.*, **41**, 4321 (1908).

(11) Fieser and Fieser, THIS JOURNAL, **57**, 782 (1935).

Anal.[12] Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81. Found: C, 76.93; H, 6.71.

2,4,6-Trimethyldiazodesoxybenzoin.—The procedure was similar to that described by Smith and Hoehn[9] for the preparation of azibenzil. Five grams of mesityl phenyl diketone monohydrazone was finely ground in a mortar with 8 g. of yellow mercuric oxide and 4 g. of anhydrous calcium sulfate. This mixture was stirred for six hours with 100 cc. of dry benzene and 0.5 cc. of saturated alcoholic potassium hydroxide solution. The resulting yellow solution was filtered by gravity and the residue washed with benzene until the washings came through colorless. Removal of the benzene left the diazo compound as a residue. It separated from dry ether in orange plates; m. p. 94–95°; yield 60%.

Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.27; H, 6.11. Found: C, 77.47; H, 6.32.

Mesitylphenylketene.—(A) The 2,4,6-trimethyldiazodesoxybenzoin was transformed into the corresponding ketene by a modification of the method of Smith and Hoehn[9] for diphenylketene. A solution of the azibenzil, prepared by the above procedure from 6 g. of monohydrazone, was distilled from a 15-cc. modified Claisen flask. After the solvent had been removed, nitrogen was introduced and the ketene distilled under reduced pressure. It was a bright yellow oil; b. p. 149–150° (12 mm.); yield 35%.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found: C, 85.17; H, 6.98.

(B) To a solution of 31 g. of pure, dry mesitylphenylacetic acid in 250 cc. of benzene at 0° was added 8.6 cc. of thionyl chloride. The reaction flask was connected to a condenser by means of a ground-glass joint and 0.5 cc. of pyridine was added dropwise. The solution was allowed to attain room temperature and was then heated slowly to boiling. Heating under reflux was continued for four hours. During this period pyridine hydrochloride collected on the walls of the flask. The solvent was removed on the pump and the residue distilled. The ketene was collected as a golden yellow oil which turned red when allowed to stand; b. p. 125–126° (2 mm.); yield 78%. It gave a negative test for chlorine but reduced an alcoholic solution of silver nitrate.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found: C, 85.68; H, 6.96.

The purest sample of the ketene to be encountered[13] was made in an attempt to reduce mesitylphenylacetyl chloride by the Rosenmund method.[14] The procedure was based on that of Barnes for mesitaldehyde.[15] It was noted that hydrogen chloride evolved steadily during the first ten hours of the introduction of hydrogen. The ketene, evidently formed by catalytic dehydrochlorination of the acid chloride, boiled at 141–142° (4 mm.); $n^{24}\text{D}$ 1.5860.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.40; H, 6.83. Found: C, 86.61; H, 6.89.

The Diacetate of Mesitylphenylketene.[8]—A mixture of 1 g. of the ketene, 10 cc. of pyridine and 10 cc. of acetic anhydride was allowed to stand for twenty-four hours. The acetate, isolated by conventional procedures, crystallized from methanol; m. p. 112–113°.

Anal. Calcd. for $C_{21}H_{20}O_4$: C, 74.98; H, 5.99. Found: C, 74.61; H, 6.61.

The ketene was found to give no gas in the Grignard machine[16] and to use 0.92 mole of reagent. The product of this reaction melted at 82–83° and was shown by the method of mixed melting points to be 1-mesityl-1-phenylpropanone.[17]

***n*-Butyl Mesitylphenylacetate.**—Four grams of the ketene was added to a mixture of 5.4 g. of dry sodium methoxide and 100 cc. of anhydrous 1-butanol. The mixture was prepared and allowed to stand for forty hours under nitrogen. The products were isolated in the usual way. In addition to a small amount of mesitylphenylacetic acid, there was isolated *n*-butyl mesitylphenylacetate; b. p. 185–187° (6 mm.); $n^{20}\text{D}$ 1.5452.

Anal. Calcd. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.30; H, 8.39.

Isopropyl Mesitylphenylacetate.—Treatment with sodium isopropoxide converted the ketene into a mixture of products from which were isolated mesitylphenylacetic acid and its isopropyl ester. The latter was recrystallized from ethanol; m. p. 65–66°.

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.17. Found: C, 81.25; H, 8.20.

Mesitylphenylacetamide.—A solution of 1 g. of mesitylphenylketene in 50 cc. of dry ether was saturated with dry ammonia. The flask was sealed and allowed to stand for six hours. The ether solution was washed successively with dilute potassium carbonate solution, water, dilute hydrochloric acid and water, and dried over calcium chloride. Evaporation of the solvent left 0.4 g. of the amide. It crystallized from dilute ethanol in white needles; m. p. 146–147°. The amide was identified by a mixed melting point with a sample made by the action of ammonia on mesitylphenylacetyl chloride.

Anal. Calcd. for $C_{17}H_{19}ON$: C, 80.63; H, 7.57. Found: C, 80.53; H, 7.72.

Mesitylphenylacetic Acid.—(A) A mixture of 0.5 g. of mesitylphenylketene, 10 cc. of water and 15 cc. of ether was allowed to stand for fifteen minutes. Thirty cubic centimeters of ether was added and the solution extracted three times with dilute potassium carbonate solution. Acidification of the carbonate solution yielded 0.5 g. of mesitylphenylacetic acid; m. p. 171–172°. This melting point agrees with that reported by Maxwell and Adams[18] and Weinstock and Fuson.[19]

(B) To a mixture of 152 g. of mandelic acid and 400 cc. of mesitylene was added, with stirring, 390 g. of anhydrous stannic chloride. During the addition, which required eighty minutes, the reaction mixture was kept at 65–75°. It was stirred for an additional six hours at 75° and allowed to stand overnight at room temperature. After the mixture had been decomposed with ice water 1500 cc. of ether was added to the organic layer. The ethereal solution was washed with water and extracted with 100-cc. portions of an 8% solution of equal parts of potassium carbonate and sodium carbonate. At first the addition of the carbonate caused the precipitation of stannic hydroxide, and the first five extracts were kept separate from the remaining nine. The latter, when acidified, yielded 150 g. of colorless acid melting at 170–172°. After one recrystallization from a mixture of 800 cc. of ethanol and 100 cc. of water, the acid melted at 173–174° and weighed 125 g. By acidification of the first five fractions, triturating the impure product with concentrated hydrochloric acid and repeating the selective extraction of its ethereal solution with carbonate solution, an additional 30 g. of pure acid was obtained. The total yield was 61%.

Condensation of Mesitylphenylketene with Mesitylmagnesium Bromide.—A solution of 8 g. of the ketene in 15 cc. of dry ether was added dropwise to an ethereal solution of mesitylmagnesium bromide, prepared from 1.52 g. of magnesium, 12.6 g. of bromomesitylene and 50 cc. of dry ether. The resulting solution was heated under reflux, with stirring, for three hours.

1,2-Dimesityl-2-phenylvinyl Alcohol.—One-half of the enolate solution was poured into an ice-concentrated hydrochloric acid mixture. The vinyl alcohol separated from ethanol in white crystals; m. p. 139–140°; yield 4 g.

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[12] The microanalyses reported in this paper were carried out by Miss Theta Spoor, Miss Margaret McCarthy, Miss Dorothy Schneider and Miss Lillian Hruda.

[13] This experiment was carried out by Dr. Norman Rabjohn.

[14] Rosenmund, *Ber.*, **51**, 585 (1918); Rosenmund and Zetzsche, *ibid.*, **54**, 425 (1921).

[15] "Organic Syntheses," **21**, 110 (1941).

[16] Kohler and Richtmyer, THIS JOURNAL, **52**, 3736 (1930).

[17] A description of this compound will be presented elsewhere.

[18] Maxwell and Adams, THIS JOURNAL, **52**, 2959 (1930).

[19] Weinstock and Fuson, *ibid.*, **58**, 1233 (1936).

Anal. Calcd. for $C_{26}H_{28}O$: C, 87.59; H, 7.92. Found: C, 87.97; H, 7.76.

1,2-Dimesityl-2-phenylvinyl Acetate

(A) The High-Melting Acetate.—To the remainder of the enolate solution was added dropwise a solution of 4 cc. of acetyl chloride in 10 cc. of ether. The resulting mixture was heated under reflux for fifteen minutes and poured on an ice-hydrochloric acid mixture. The acetate was recrystallized from a mixture of 50 cc. of absolute ethanol and 5 cc. of *n*-butyl alcohol. After two such recrystallizations the compound melted at 179.5–180.5° (cor.); yield 2 g.

Anal. Calcd. for $C_{28}H_{30}O_2$: C, 84.38; H, 7.59. Found: C, 84.38; H, 7.79.

Hydrolysis.—Hydrolysis of this acetate was carried out in two ways.

(a) The acetate (0.35 g.) was covered with 13 cc. of absolute ethanol, and 0.7 cc. of concentrated hydrochloric acid was added. The mixture was heated under reflux for eleven hours. The volume of the solution was reduced by evaporation to approximately 4 cc. and five drops of water were added. The crystals of 1,2-dimesityl-2-phenylvinyl alcohol obtained in this way melted at 138–139° and did not depress the melting point of an authentic sample of this compound.

(b) The acetate (0.31 g.) was covered with a solution of 1 g. of potassium hydroxide and 10 cc. of methanol, and the mixture was heated under reflux for forty-five minutes. The solution was poured into 25 cc. of water and the product, 1,2-dimesityl-2-phenylvinyl alcohol, was purified in the usual way; m. p. 139–140°. A similar experiment in which, however, the reaction mixture was not heated but was kept at 0–5°, for twelve days, yielded the same vinyl alcohol.

(B) The Low-Melting Acetate.—A solution of 0.35 g. of 1,2-dimesityl-2-phenylvinyl alcohol, 4.5 cc. of dry pyridine and 1.9 cc. of acetic anhydride was heated under reflux for twenty minutes and poured into 50 cc. of water. The acetate was purified by recrystallization from ethanol; m. p. 160–161°.

Anal. Calcd. for $C_{28}H_{30}O_2$: C, 84.38; H, 7.59. Found: C, 84.55; H, 7.83.

The low-melting acetate was made also from α-phenyl desoxymesitoin. A solution consisting of 5 g. of the ketone, 30 cc. of anhydrous *n*-butyl ether and 15 cc. of toluene was added to a methylmagnesium iodide solution containing about twice the amount of reagent required to enolize the ketone. The ether was removed by distillation in a stream of dry nitrogen and the reaction mixture was kept under nitrogen for six hours in an oil-bath maintained at 160°. The solution was cooled and a solution of 3.5 cc. of acetyl chloride in 20 cc. of dry ether was added dropwise. After the reaction mixture had been heated under reflux for one hour it was decomposed in the usual way. The acetate melted at 158–160°.

Hydrolysis of this ester by the first procedure outlined above for the isomeric acetate produced 1,2-dimesityl-2-phenylvinyl alcohol; m. p. 138–139°. Low temperature saponification yielded the same result.

Mesitylphenylacetyl Chloride.—A mixture of 12 g. of mesitylphenylacetic acid (m. p. 172–173°), 30 cc. of thionyl chloride and 10 cc. of dry chloroform was warmed to effect solution and allowed to stand for thirteen hours at room temperature. After the solution had been maintained at 50° for fifteen minutes under slightly diminished pressure the solvent was distilled on the water pump. The acid chloride was purified by recrystallization from a mixture of 80 cc. of low-boiling petroleum ether and 30 cc. of high-boiling petroleum ether; m. p. 88–89°; yield 84%.

Anal. Calcd. for $C_{17}H_{17}OCl$: C, 74.84; H, 6.29. Found: C, 74.82; H, 6.48.

α-Phenyldesoxymesitoin.—A solution of mesitylmagnesium bromide containing about 0.08 mole of reagent was added, dropwise and with stirring, to a solution of 23 g. (0.08 mole) of mesitylphenylacetyl chloride in 100 cc. of dry ether. After the mixture had been heated under reflux, with stirring, for ninety minutes it was decomposed in the usual way. Six grams of mesitylphenylacetic acid was recovered. The α-phenyldesoxymesitoin was recrystallized from a mixture of equal volumes of absolute ethanol and dry *n*-butyl ether; m. p. 163–164°; yield 10 g.

Anal. Calcd. for $C_{26}H_{28}O$: C, 87.59; H, 7.92. Found: C, 87.44; H, 7.97.

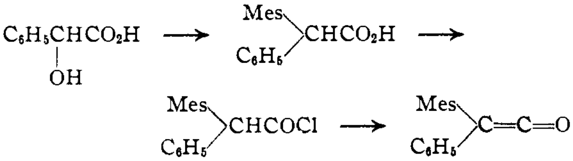
α-Phenyldesoxymesitoin was made also by the condensation of α-chlorophenylacetyl chloride with mesitylene by the Friedel–Crafts method. A solution of 24 g. of the acid chloride in 50 cc. of mesitylene was added, dropwise and with stirring, over a forty-five minute period to a mixture of 41 g. of anhydrous aluminum chloride and 80 cc. of mesitylene. The temperature of the reaction mixture was kept at 30–35° during the mixing and at 65° for four hours afterward. The mixture was decomposed in the usual way. After one recrystallization from ether the ketone melted at 157–160° and weighed 15 g. After one recrystallization from 1-butanol the compound melted at 162–164°.

In an attempt to form an acetate the ketone was heated under reflux for twenty-five minutes with a mixture of 1.8 cc. of acetic anhydride and 4.5 cc. of dry pyridine. The ketone was recovered unchanged.

Enolization of the ketone was effected by heating it (0.3 g.) under reflux for twelve hours with a solution of 0.8 g. of sodium in 20 cc. of absolute ethanol. The 1,2-dimesityl-2-phenylvinyl alcohol produced in this way melted at 138–140°.

Summary

A satisfactory synthesis of mesitylphenylketene from mandelic acid and mesitylene has been developed. It consists of the following steps.



$$C_6H_5\underset{\displaystyle OH}{\underset{|}{C}}HCO_2H \longrightarrow \begin{matrix}Mes\\C_6H_5\end{matrix}\!\!>CHCO_2H \longrightarrow \begin{matrix}Mes\\C_6H_5\end{matrix}\!\!>CHCOCl \longrightarrow \begin{matrix}Mes\\C_6H_5\end{matrix}\!\!>C{=}C{=}O$$

Condensation of the ketene with mesitylmagnesium bromide has been shown to yield the stable vinyl alcohol, 1,2-dimesityl-2-phenylvinyl alcohol.

The corresponding ketone, α-phenyldesoxymesitoin, has been produced by the reaction of mesitylphenylacetyl chloride with mesitylmagnesium bromide and by the condensation of mesitylene with α-chlorophenylacetyl chloride in the presence of aluminum chloride. It was isomerized to the vinyl alcohol by treatment with sodium ethoxide.

URBANA, ILLINOIS

RECEIVED JUNE 8, 1944