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THE PREPARATION OF
\[ \beta-\{5-(p-\text{HYDROXYPHENYL})-\text{CYCLOHEXANEDIONE- 1,3}\}-\text{ALANINE} \]

BY

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A THESIS

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INTRODUCTION
For several years, much of the organic work performed in this laboratory has been centered around derivatives of 5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanonedione-1,3 which have resemblance to compounds of physiological importance.

The above mentioned cyclohexanedione compound was first synthesized by Papadakis\(^1\) in 1945 to be used as a possible stepping stone for synthesis of compounds which are similar in structure and functional groups to the cardiac glycosides.

Later, in 1953, Papadakis, Scigliano, and Pirruccello\(^2\) prepared various acylation products of 5-(p-acetoxyphenyl)-4,6-dicarbethoxycyclohexanonedione-1,3

\[
\text{\includegraphics[width=0.5\textwidth]{image}}
\]

where \(R=\text{COCH}_3, \text{COCH}_2\text{H}_5, \text{COCH}_2\text{CH}_2X, \text{COCH}_2\text{CH}_2\text{COOCH}_3\).

These compounds with C-acylation at the 2-position are structurally similar to usnic acid and chalcones, both of which show antibiotic activity against human


and bovine tubercle bacilli.

Similarly, reaction of the sodio derivative of the above compound with p-acetaminobenzenesulfonyl chloride gave a sulfone product. 3

\[ \text{R} \quad \text{O} \quad \text{C} \quad \text{O} \quad \text{C} \quad \text{O} \quad \text{SO}_2 \quad \text{N} \quad \text{C} \quad \text{H}_3 \]

The possibility of physiological activity in this case is enhanced by the fact that p-acetaminobenzene sulfones have been used in the therapy of tuberculosis and leprosy.

Also in 1953, Papadakis and Scigliano 4 prepared 5-(p-hydroxyphenyl)-4,6-dicarboxy-2-(β-diethylamino-propanol)-cyclohexanedione-1,3.

\[ \text{HO} \quad \text{C} \quad \text{O} \quad \text{C} \quad \text{O} \quad \text{C} \quad \text{H}_2 \quad \text{CH}_2 \quad \text{N} \quad \text{C}_2 \text{H}_5 \]

The interest in such a compound was due to the fact that many substituted diethylaminoalkanols have antimalarial properties.

In the further search for compounds of possible

---

3 Ibid.

derivative of 5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclo-
hexanedione-1,3 was considered. Such a compound could
serve as the basis for further important work. The
object of this thesis, therefore, is the synthesis of
$\beta-[5-(p\text{-hydroxyphenyl})\text{-cyclohexanedione-1,3}]$-alanine.
GENERAL DISCUSSION
One possible method of preparation of \( \beta-[5-(p\text{-hydroxyphenyl})\text{-cyclohexanedione-1,3}] \)-alanine is formation of a Mannich base of 5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3, followed by reaction with acetamino diethyl malonate. The resulting compound is then saponified, decarboxylated, and hydrolyzed to the amino acid. The sequence of reactions is as follows.

\[
\begin{align*}
\text{HO} & \quad \text{C} \quad \text{H} \\
\text{C} & \quad \text{OR} \\
\text{C} & \quad \text{OR}
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \quad \text{C} \quad \text{C} \quad \text{OR} \\
\text{H} & \quad \text{C} \quad \text{OR} \\
\text{C} & \quad \text{OR}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{C} \quad \text{CH}_2 \quad \text{C} \quad \text{OR} \\
+ & \quad \text{C}_2\text{HSO}_3\text{Na} \\
\rightarrow & \quad \text{CH}_3 \quad \text{C} \quad \text{C} \quad \text{OR}
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \quad \text{C} \quad \text{H} \\
\text{C} & \quad \text{OR} \\
\text{C} & \quad \text{OR}
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \quad \text{C} \quad \text{C} \quad \text{OR} \\
\text{H} & \quad \text{C} \quad \text{OR} \\
\text{C} & \quad \text{OR}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{C} \quad \text{CH}_2 \quad \text{C} \quad \text{OR} \\
+ & \quad \text{C}_2\text{HSO}_3\text{Na} \\
\rightarrow & \quad \text{CH}_3 \quad \text{C} \quad \text{C} \quad \text{OR}
\end{align*}
\]
\[ \text{HO-} \rightarrow \begin{array}{c} \text{CH}_3- \text{C} \text{- N} \text{- CH}_2- \text{N} \text{- C}_2 \text{H}_5 \end{array} \quad (\text{III}) \]

\[ + \begin{array}{c} \text{CH}_3-\text{C} \text{- N} \text{- CH} \text{- H} \end{array} \rightarrow \begin{array}{c} \text{COOC}_2 \text{H}_5 \end{array} \]

\[ \rightarrow \]

\[ \begin{array}{c} \text{HO-} \\text{CH}_2- \text{C} \text{- N} \text{- C} \text{- CH}_3 \end{array} \quad (\text{IV}) \]
Saponification and Hydrolysis → 

\[
\text{HO-} \quad \text{CH}_2-\text{C-}\text{NH-CH}_2-\text{COOH} \quad \text{COOH}
\]

→ 

\[
\text{HO-} \quad \text{CH}_2-\text{C-}\text{NH-CH}_2-\text{COOH} \quad \text{COOH}
\]

→ 

\[
\text{HO-} \quad \text{CH}_2-\text{C-}\text{NH-CH}_2-\text{COOH} \quad \text{COOH}
\]

→ 

\[
\text{HO-} \quad \text{CH}_2-\text{C-}\text{NH-CH}_2-\text{COOH} \quad \text{COOH}
\]
The synthesis of 5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 (II), was performed by following, in general, the procedures outlined by Papadakis.\(^5\)

The synthesis of 2-(diethylaminomethyl)-5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 (III) involves a standard Mannich reaction which consists in condensation of ammonia or a primary or secondary amine with formaldehyde and a compound containing an active hydrogen.\(^6\) In this case, the dione compound (II) should easily react since it has a methylene center whose hydrogen atoms are strongly activated by the two neighboring carbonyl groups.

Some difficulties may tend to arise, however, in the synthesis of the Mannich compound (III) since at least two possible concurrent side reactions may result. The first one involves tautomerism of one of the active hydrogens on the cyclohexane ring followed by reaction of the diethylamine, with removal of one molecule of water.

\(^5\)Papadakis, *loc. cit.*

An analogous reaction with dry ammonia was performed by Pirruccello resulting in a NH$_2$ group in place of the N(C$_2$H$_5$)$_2$ group.\textsuperscript{7}

The other possible side reaction is the formation of a bis compound with the formaldehyde and two molecules of the dione compound. Papadakis reported such a compound in 1953.\textsuperscript{8}

---

\textsuperscript{7}Pirruccello, Unpublished Master of Science Thesis, Creighton University (1952).

If the addition of reagents is done, however, in such a way as to have the diethyl amine always present in excess, and if the formaldehyde and dione compound are added in small portions over a period of time, then the above side reactions should be averted, and the Mannich compound should be the predominant product.

It is stated in *Organic Reactions*, Vol. I,\(^9\) that the common practice is to use 1.00 molecular equivalent of the carbonyl compound, 1.05-1.10 equivalents of the amine, and 1.5-2.0 equivalents of formaldehyde.

F. F. Bliche, in *Organic Reactions*, Vol. I,\(^10\) reports that another possible side product is \(N, N'-\)tetraethyl methylenediamine formed by condensation of two molecules of diethylamine and one molecule of formaldehyde.


\(^10\)Ibid., p.329.
The subsequent reactions upon the Mannich compound (III) follow the general procedures used in the modified malonic ester synthesis of tryptophan by Snyder and coworkers.\textsuperscript{11, 12} The general reactions involved in their work are as follows:

\[
\begin{align*}
C_2H_5 - N^H + CO + H-N \rightarrow C_2H_5 - N^H \quad (C_2H_5 - N^H) + H_2O
\end{align*}
\]


\text{Saponification and Hydrolysis} \\
\text{\textbf{C}} \\
\text{\textbf{D}} \\
\text{\textbf{E}} \\
\text{\textbf{F}}
The starting material, indole, was reacted with formaldehyde and dimethylamine to form gramine (B). The gramine then was reacted with acetamino diethylmalonate to form ethyl-α-acetamino-α-carbethoxy-β-(3-indole)-propionate (C). The best results, state the authors, were obtained (90%) when the reactants were refluxed for at least 5 hours in an inert solvent such as toluene or xylene in the presence of powdered sodium hydroxide. Nitrogen gas was passed through the mixture to sweep out the dimethylamine which was evolved. The product precipitated upon cooling for several hours.

Next, saponification of the ester (C) with NaOH for four hours, followed by acidification with cold HCl, yielded α-acetamino-α-carboxy-β-(3-indole)-propionic acid (D).

The crude acid (D) was heated under reflux with water for 2.5 hours for decarboxylation to N-acetyl-tryptophan (E). Alkaline hydrolysis of this product for 20 hours followed by acidification with glacial acetic acid yielded the desired amino acid, tryptophan (F).

The above type of synthesis was applied for the preparation of β-[5-(p-hydroxyphenyl)-cyclohexanedione-1,3]-alanine, since after obtaining the Mannich compound
(III), the subsequent reactions are the same. The general scheme of the synthesis appears in the flow sheet of reactions in the general discussion on pages 6-9, and the details of the procedure and results are given in the experimental part of this paper.

Another possible method of synthesis of this amino acid is through condensation of the aldehyde of 5-(p-hydroxyphenyl)-cyclohexanedione-1,3 with 2,5-diketopiperazine.

\[
\begin{align*}
\text{(1) } & \text{HI, P} \\
\text{(2) } & \text{Hydrolysis} \\
\end{align*}
\]
Reduction of the double bonds of the intermediate product with HI and phosphorous, followed by hydrolysis would yield two molecules of $\beta$-[5-(p-hydroxyphenyl)-cyclohexanedione-1,3]-alanine. This particular method of synthesis has been used successfully in the preparation of phenylalanine and tyrosine.\textsuperscript{13}

Difficulties were encountered, however, in attempting to synthesize the aldehyde necessary in this particular synthesis problem.

The first method which was attempted was reaction of 5-(p-acetoxyphenyl)-4,6-dicarbethoxy-1,3-cyclohexanedione with ethyl formate in the presence of sodium ethoxide.

\[ \text{AcO} \text{C} \text{O} \text{R} \text{C} \text{O} \text{R} \text{C} \text{O} \text{R} \text{C} \text{O} \text{R} \text{C} \text{C} \text{O} \text{H} + \text{C}_2\text{H}_5\text{O}-\text{C}-\text{H} \xrightarrow{\text{NaOCC}_2\text{H}_5} \]

\[ \text{AcO} \text{C} \text{O} \text{R} \text{C} \text{O} \text{R} \text{C} \text{O} \text{R} \text{C} \text{C} \text{O} \text{H} + \text{C}_2\text{H}_5\text{OH} \]

Four trials were made on this method with variations in the conditions and solvents. However, no distinct success was obtained, quantitatively speaking, although in each trial, positive test for presence of aldehyde with Fehling solution was obtained, indicating that some aldehyde probably was formed.

Another type of aldehyde synthesis which was attempted was the reaction of 5-(p-acetoxyphenyl)-4,6-dicarboxylohexanedione-1,3 with dimethylformamide and phosphoryl chloride.

\[
\begin{align*}
\text{CH}_3 - \text{N} - \text{C} = \text{O} & \quad + \quad \text{POCl}_3 \\
\text{CH}_3 & \quad \rightarrow \quad \left[ \begin{array}{c}
\text{CH}_3 - \text{N} - \text{C} = \text{O} \\
\text{H} \\
\text{POCl}_3
\end{array} \right] \\
& \quad + \quad \text{Aco} - \quad \begin{array}{c}
\text{COOR} \\
\text{COOR}
\end{array} \\
& \quad \rightarrow \quad \begin{array}{c}
\text{Aco} - \\
\text{COOR} \\
\text{COOR}
\end{array} \\
& \quad \begin{array}{c}
\text{CH}_3 - \text{N} - \text{C} = \text{O} \\
\text{H_2O} \\
\text{NaOAc}
\end{array} \\
& \quad \rightarrow \quad \begin{array}{c}
\text{CH}_3 \\
\text{CH}_3
\end{array} \\
& \quad \begin{array}{c}
\text{POCl}_2 \\
\text{O}
\end{array} \\
& \quad \begin{array}{c}
\text{HCl}
\end{array} \\
& \quad \begin{array}{c}
\text{H}_2\text{O}
\end{array} \\
& \quad \begin{array}{c}
\text{NaOAc}
\end{array}
\end{align*}
\]
The first step involves the formation of dimethylformamide-phosphoryl chloride complex which would be expected to react with the active methylene group of the dione compound. The resulting compound, upon hydrolysis and neutralization with sodium acetate, would yield the desired aldehyde. Both p-dimethylaminobenzaldehyde\(^ {14}\) and 2-pyrrolealdehyde\(^ {15}\) have been prepared from dimethylaniline and pyrrole respectively by this same method.

Again, the results were not very successful, although a Fehling solution test did show the presence of some aldehyde. More details on these two aldehyde synthesis attempts are given in the experimental part of this paper. Further investigation for successful application of these methods will be carried on in the future.


The preparation of 5-(p-hydroxyphenyl)-4,6-dicarbethoxy-cyclohexanedione-1,3 and the foregoing intermediate compounds, was carried out, in general, according to the known procedures of Papadakis\textsuperscript{16} along with some more recent modifications.

**PREPARATION OF ETHYL-[p-HYDROXYBENZYLIDENE]-MALONATE (I)**

Five hundred grams of p-hydroxybenzaldehyde was placed in a 3 liter 3 necked flask equipped with reflux condenser and stirring motor. Along with 30 ml of piperidine, was also added 625 ml (4.1 m) of diethyl malonate. The mixture was heated with a water bath for a total of 9 hours. The dark viscous liquid was then poured into a large beaker and placed in the refrigerator overnight to cool. A few crystals were formed by the following morning and after stirring and cooling again, a solid mass of crystals was obtained.

The yellow crystals of ethyl-[p-hydroxybenzylidene]-malonate were filtered with suction and dried. The dark mother liquor was refrigerated again and another crop of crystals was obtained. Total yield of the crude product was 691.6 g (2.62 m).

\textsuperscript{16}Papadakis, \textit{loc. cit.}
PREPARATION OF 5-(p-HYDROXYPHENYL)-4,6-DICARBETHOXYCYCLOHEXANEDIONE-1,3 (II)

In a 3 neck 3 liter flask equipped with stirrer and reflux condenser, 60.3 g (2.62 m) of sodium metal was dissolved in absolute alcohol. Next 364 g (2.80 m) of ethyl acetoacetate was added to the flask along with 691 g (2.62 m) of ethyl-[p-hydroxybenzylidene]-malonate. Almost immediately a bright yellow material formed and more alcohol was added to help mix the solution. The material was refluxed with a water bath for four hours and then most of the excess alcohol was distilled from the reaction mixture. This mixture was then poured into large beakers and water was added until the product was dissolved. This solution was diluted out three times the original volume and 3 N HCl was added slowly with stirring. White crystals were formed which were filtered and then dried. The dried product was dissolved in methyl alcohol under reflux. Water was added to cloudiness and after refluxing a short time longer, the solution was boneblackened and filtered while hot. The dark filtrate was cooled and the crystals which formed were filtered and washed immediately with ether. The dried product melted at 201-202° C.
PREPARATION OF 2-(DIETHYLAMINOMETHYL)-5-(p-HYDROXY-PHENYL)-4,6-DICARBETHOXYCYCLOHEXANEDIONE-1,3 (III)

Forty-one grams of 5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 was just covered with dioxane in a flask. Eighteen ml of diethylamine was mixed with 8.8 ml of 40% formaldehyde and this solution was poured immediately in the flask containing the dioxane and dione compound. Upon shaking, the solid material dissolved and the solution was heated on a hot plate for 15-20 minutes. The white precipitate which formed was filtered and washed with some dioxane and ether. The melting point was 191° C. and the material gave a positive test for nitrogen. The product was identical with that prepared previously by Papadakis.¹

Anal. Calc. for C₂₈H₃₁O₇N₄H₈O: C, 62.43; H, 7.24
Found: C, 62.43; H, 7.04

Preparation of Ethyl-α-Acetamo-α-Carbethoxy-β-[5-(p-HydroxypheNyl)-4,6-DicarbethoxyCyclohexanedione-1,3]-Propionate (IV)

A 500 ml 3 neck flask was equipped with a condenser, electric stirrer, and mercury seal, and the following materials were mixed in 175 ml of dioxane: 40 g

¹P. E. Papadakis, Private Communication.
(0.092 m) of the Mannich compound (flowsheet formula III), 19.96 g (0.092 m) of acetamino diethyl malonate, 4 g (0.1 m) of sodium hydroxide. The white pasty mixture was refluxed with a heating mantle for 9 hours. During this time nitrogen gas was passed through the mixture to sweep out the diethylamine which was formed from the reaction. Toward the end of the reflux period, a piece of damp litmus paper placed at the open end of the condenser no longer turned blue, indicating that no more diethylamine was being liberated.

The white crystalline product was filtered, washed with ethyl ether, and dried. Since it was soluble in water and did not appear to have a melting point or decomposition point, the product was assumed to be a sodio derivative of (IV), and was used directly in the next step. For the analytical sample, however, some of the sodio compound was dissolved in water and a white, tacky material was precipitated upon dropwise addition of 6 N HCl. This material was washed several times with water, and was crystallized on a porous plate. M. P. 95-100° C. and rose in the tube.

Anal. Calcd. for C_29H_35O_13N:  C, 58.23;  H, 5.89

Found:  C, 58.14;  H, 6.07
PREPARATION OF N-ACETYL-β-[5-(p-HYDROXYPHENYL)-CYCLOHEX-
ANEDIONE-1,3]-ALANINE (VI)

Twenty-six grams (0.65 m) of NaOH was dissolved in 100 ml of water along with 53.26 g (0.093 m) of the sodio derivative of compound (IV). The dark solution was refluxed with a heating mantle for 23 hours. After cooling, the solution was neutralized with con. HCl using litmus paper as an indicator. The temperature did not rise above 25° C. during the neutralization. At the neutral point only a small quantity of material was precipitated. The material was filtered off and the filtrate was evaporated on a hot plate to a gummy crystalline mass which was extracted several times with absolute alcohol. The white crystalline residue that did not dissolve in the cold alcohol weighed 56.8 g. It was a mixture of NaCl and the product α-acetamino-
α-carboxy-β-[5-(p-hydroxyphenyl)-4,6-dicarboxycyclohex-
anedione-1,3]-propionic acid (V).

The next step involved decarboxylation of the acid (V) to N-acetyl-β-[5-(p-hydroxyphenyl)-cyclohex-
anedione-1,3]-alanine (VI). A solution of 56.8 g (0.12 m) of (V) dissolved in 250 ml of water and 7 ml of con. HCl was refluxed with a heating mantle for approximately 35 hours, cooled, and neutralized with 6 N NaOH. Product (VI) was soluble in water.
PREPARATION OF $\beta$-\(5\)-(p-HYDROXYPHENYL)-CYCLOHEXANE-DIONE-1,3\]-ALANINE (VII)

The neutral solution of the decarboxylated product (VI) was made strongly basic with 16 g of NaOH dissolved in 75 ml of water to facilitate the hydrolysis of the acetamino group. The solution was refluxed with a heating mantle for 36 hours. By the end of this time, some white material had precipitated out. After cooling, the solution was neutralized with HCl, and a copious white precipitate formed. The material was filtered and washed with cold water and then absolute alcohol. The dried white product, which appeared to be insoluble in water, weighed 12.69.

The original filtrate was evaporated to a small volume and upon cooling another crop of crystals was obtained. The material was filtered and washed with absolute alcohol. The yield of this water soluble product was 30.9 g. Neither of the two crops of material gave the correct analysis for carbon and hydrogen, and this fact was attributed to the inability to isolate a pure analytical sample of the amino acid.

Qualitative evidence for the presence of the amino acid was found, however, when the material was tested with ninhydrin. A red-violet color was obtained, which is a specific test for an alpha amino acid.
Since \( \beta-[5-(p\text{-hydroxyphenyl})\text{-cyclohexanедione-1,3}] \)-alanine would have a structural resemblance to tyrosine, it was thought that the chromatographic \( R_F \) values of the two amino acids should be somewhat similar. Paper chromatography experiments showed this fact to be true.

Strips of chromatography paper were spotted with a sample of tyrosine in a phenol-saturated aqueous solution, and a sample of the above water soluble material dissolved in water. The solvent used was water saturated with phenol. The strips were developed for 2-3 hours, dried, and sprayed with 0.5% ninhydrin in butanol. Upon heating the strips, two definite colored spots were obtained. The \( R_F \) value for tyrosine was 0.79 and that of the assumed \( \beta-[5-(p\text{-hydroxyphenyl})\text{-cyclohexanедione-1,3}] \)-alanine was 0.84. Duplicate results were obtained on similar trials.

**TWO ATTEMPTED PREPARATIONS OF 2-FORMYL-5-(p-ACETOXYPHENYL)-4,6-DICARBOXYCICLOHEXANEDIONE-1,3**

**A. ETHYL FORMATE METHOD**

A 500 ml 3 neck flask was fitted with a mercury seal stirrer, and a condenser with a \( \text{CaCl}_2 \) drying tube at the top. Two grams (0.087 m) of sodium metal was
dissolved in absolute ethyl alcohol and the resulting
sodium ethoxide solution was added to the flask along
with 14.47 g (0.037 m) of 5-(p-acetoxyphenyl)-4,6-
dicarbethoxyphenoxyhexanediione-1,3, 9.24 g (0.124 m) of
ethyl formate, 55 ml of dioxane and approximately
50 ml of alcohol. The white-gray mixture was refluxed
for a total of 11 hours with a hot water bath. (After
3 hours of reflux, 6 ml more of ethyl formate were
added).

The white mass was filtered (the filtrate was
saved), dried, and washed with HCl solution to neutralize
any sodium ethoxide present. The material was then
filtered and washed with water and dried. The melting
point of the crude product was 197-200° C. and upon
recrystallization from methanol and water, the melting
point was 202-203°. Since this melting point is
comparable to that of the original dione compound and
since this material did not give a positive aldehyde
test with Fehling solution, it was assumed that this
material did not react.

The filtrate from the first filtration which, as
stated above, was saved, was evaporated on a hot plate
to a syrupy reddish residue. The residue was extracted
several times with ether and the ether extracts, upon
evaporation of the ether, yielded some bright yellow crystals. These did give a positive aldehyde test. The m.p. was 174-180° C.

B. DIMETHYLFORMAMIDE-PHOSPHORYL CHLORIDE METHOD

In a 200 ml 3 neck flask equipped in the usual manner (stirrer, mercury seal, condenser, CaCl₂ drying tube) was placed 10 ml of cold dimethylformamide. With additional cooling, 1.53 g (0.01 m) of phosphoryl chloride was added dropwise over a period of 20 minutes to the flask with stirring. Next 3.9 g (0.01 m) of 5-(p-acetoxyphenyl)-4,6-dicarbethoxy cyclohexanedione-1,3 was dissolved in 10 ml of dimethylformamide and this solution was added dropwise with stirring and cooling to the dimethylformamide-phosphoryl chloride complex. The resulting clear green solution was then refluxed over a hot water bath for 2.5 hours. At the end of this time the clear red solution was cooled and poured over cracked ice with stirring. Neutralization of the solution was first attempted with a saturated sodium acetate solution, but NaOH solution was used toward the end. The temperature was kept between 0-10° C. Some reddish tacky material, which was insoluble in the aqueous solution, was formed and this was separated, dissolved in 25 ml of 95% ethyl alcohol, and made basic
with 6 N NaOH. The muddy brown solution was warmed on a hot plate, cooled, and an equal volume of ethyl ether was added. Next 6 N HCl was added with stirring and the resulting white-gray crystals were filtered and washed with ether. The crystals did not melt and gave a fair test for aldehyde with Fehling solution.
1. 2-(Diethylaminomethyl)-5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 was prepared.

2. Ethyl-α-acetamino-α-carbethoxy-β-[5-(p-hydroxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3] propionate was prepared.

3. Qualitative evidence shows that β-[5-(p-hydroxyphenyl)-cyclohexanedione-1,3]-alanine was synthesized although the carbon and hydrogen analysis was inaccurate due to the inability to obtain a pure sample.

4. Two different methods of preparation of 2-formyl-5-(p-acetoxyphenyl)-4,6-dicarbethoxycyclohexanedione-1,3 were attempted.
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