Pelzer

The Synthesis of an Optically Active Dyestuff
THE SYNTHESIS OF AN OPTICALLY ACTIVE DYESTUFF

BY

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THESIS

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THIS IS TO CERTIFY THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Harry Louis Pelzner

ENTITLED

The Synthesis of an Optically Active Dye-stuff

IS APPROVED BY ME AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF Bachelor of Arts

Roger Adams

Instructor in Charge

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Acknowledgement

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I. Introduction.

Optical activity sometimes has a marked influence upon the physical characteristics of a compound. The differences due to optical isomerism are well known in organic chemistry, and especially in the chemistry of the amino-acids and the alkaloids. Examples of this are found in the following cases among others:

d-asparagine is a compound which has a sweet taste.
l-asparagine is sour. l-tartaric acid is twice as poisonous as the d form when fed to guinea pigs.

From these and other variations in physical properties, undoubtedly due to optical activity, the question naturally arose as to the probable effect of an optically active group upon the coloring power of dyestuffs, their affinity for the fiber, and the actual color produced by the addition of an optically active group.

The problem then may be defined as the synthesis of an organic compound having the following characteristics:

(1) A chromophore; the color bearing group selected was the di-azo group, owing to its efficiency as a color bearer, and the fact that it might be easily formed with an optically active compound as one component without serious loss of the material in the operation.

(2) An optically active group. The group selected was an asymmetric carbon atom, with the di-azo, ethyl, hydrogen, and carboxyl radicals attached to it. The carboxyl group was used, because it materially assists in the resolution of the racemic compound which is first formed. Ethyl and hydrogen radicals were used on the other two valences, because they are not readily
decomposed by fuming nitric acid. The use of fuming nitric acid was necessary in order to introduce the di-azo group.

(3) An auxochrome, or color helper. Beta napthol was selected for this portion of the compound, because of its known efficacy as an auxochrome in dyestuffs.

The plan for the synthesis is as follows:

(1) The two hydrogen atoms on the a carbon atom in acetoacetic ester are to be replaced by ethyl and benzyl groups, as follows:

\[
\text{CH}_3 \quad \text{C}=\text{O} \quad + \quad \text{NaOC}_2\text{H}_5 = \quad \text{CH}_3 \quad \text{C}=\text{O} \quad \text{ONa} + \text{C}_2\text{H}_5\text{OH}
\]

\[
\text{CH}_3 \quad \text{C}=\text{O} \quad \text{H-C-H} \quad + \quad \text{NaOC}_2\text{H}_5 \quad \text{C} = \text{O} \quad \text{OC}_2\text{H}_5
\]

\[
\text{CH}_3 \quad \text{C}-\text{ONa} \quad \text{BrC}_2\text{H}_5 \quad + \quad \text{H} = \quad \text{CH}_3 \quad \text{C}=\text{O} \quad \text{OC}_2\text{H}_5
\]
(a) Ethyl benzyl acetoacetic ester is to be saponified by sodium in absolute alcohol to form the ethyl ester of \( \alpha \)-ethyl-hydrocinnamic acid.

(b) Ethyl \( \alpha \)-ethyl hydrocinnamate is to be saponified with sodium hydroxide in order to obtain \( \alpha \)-ethyl-hydrocinnamic acid.
(3) a-ethyl-hydrocinnamic acid is to be nitrated for the purpose of preparing para-nitro-a-ethyl-hydrocinnamic acid.

(4) The nitro acid thus formed is to be combined with an optically active base, and crystallized in order to separate the optical isomers in the form of their salts. After separation, the optically active acids are to be obtained by acidification.
(5) Para-nitro-α-ethyl-hydrocinamic acid is to be reduced to para-amino-α-ethyl-hydrocinamic acid hydrochloride.

\[ \begin{align*}
\text{O} & - \text{C} - \text{C} - \text{H} \\
& \text{\underline{C}_2\text{H}_5} - \text{H} \\
\text{OH} & - \text{N} = \text{O} + 6\text{H} \\
+ & \text{HCl}
\end{align*} \]

\[ \text{O} = \text{C} - \text{C} - \text{C} \\
\text{\underline{C}_2\text{H}_5} - \text{H} \\
\text{OH} + \text{H}_2\text{O} \]

(6) Diazotization of the amine and coupling of the diazo-salt with beta-napthol.

\[ \begin{align*}
\text{O} & - \text{C} - \text{C}(\text{H})(\text{C}_2\text{H}_5) - \text{C}_2\text{H}_2 \\
\text{OH} & - \text{N} = \text{N} - \text{Cl} + 2\text{H}_2\text{O}
\end{align*} \]

(7) Physical tests to determine the optical activity of the dye, and its suitability as a dyestuff.
II- Experimental Part

Synthesis of ethyl acetoacetic ester.

Ethyl acetoacetic ester was prepared according to Vanino (1) as follows:

One mole of sodium was dissolved in alcohol in the proportions of three-hundred cubic centimeters to twenty-three grams. The acetoacetic ester, one-hundred-thirty grams (one molar), was then poured thru a reflux condenser into the cooled solution of sodium ethylate. The mixture was again cooled, and one-hundred-fourteen grams (one mole) of ethyl bromide (with five percent excess) was allowed to flow slowly into the solution of sodium acetoacetic. The mixture was then heated on the water bath until a portion of the solution on dilution with water showed a neutral or very faintly alkaline reaction. In most cases this took about two and a half hours. The alcohol was then distilled off as far as possible on the water bath; the residue poured into three-hundred cubic centimeters of water, and the layers of water and acetoacetic ethyl ester separated after thorough shaking. A little ether was now added to the water layer to remove the small amount of dissolved ester, the ethereal decoction added to the ester layer previously removed, and the whole dried over sodium sulfate and distilled. The portion boiling from 195-196 degrees was collected as pure acetoacetic ethyl ester. Yield, one-hundred-ten grams—seventy percent.

Acetoacetic ethyl ester was prepared exactly as described above in five different portions during the course of this investigation. Below is given a summary of the amounts prepared and the yields obtained:

<table>
<thead>
<tr>
<th>Amount Prepared</th>
<th>Percentage Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Amount Prepared</td>
<td>Percentage Yield</td>
</tr>
<tr>
<td>-----------------</td>
<td>------------------</td>
</tr>
<tr>
<td>40 grams</td>
<td>68 %</td>
</tr>
<tr>
<td>84 grams</td>
<td>70 %</td>
</tr>
<tr>
<td>110 grams</td>
<td>70 %</td>
</tr>
<tr>
<td>110 grams</td>
<td>70 %</td>
</tr>
<tr>
<td>231 grams</td>
<td>71 %</td>
</tr>
</tbody>
</table>

The yield according to Vanino (1), is seventy-two percent, so this agrees fairly well with his results.

Synthesis of ethyl benzyl acetoacetic ester.

Conrad-Limpach (2) and Dieckmann (3) have prepared ethyl benzyl acetoacetic ester by the interaction of ethyl iodide and sodium benzyl acetoacetic ester. It seemed better to attempt to prepare ethyl benzyl acetoacetic ester by the interaction of sodium ethyl acetoacetate and benzyl chloride, for the following reasons:

Conrad-Limpach (2) and Dieckmann (3) both state that ethyl benzyl acetoacetic ester boils under atmospheric pressure at two-hundred ninety-four--two hundred ninety-eight degrees. Since ethyl acetoacetic ester is stable under atmospheric pressure while acetoacetic ester markedly decomposes, it was reasoned that in a similar manner ethyl benzyl acetoacetic ester should be stable under atmospheric pressure while benzyl acetoacetic ester is not. If it were possible to distill ethyl benzyl acetoacetic ester from a mixture under atmospheric pressure without decomposition, a much purer product would be obtained since it would be possible to select the fractions with different boiling points more accurately.
The first attempt at preparation was carried out as follows:

Five and two-tenths grams of sodium were dissolved in one hundred twenty five cubic centimeters of absolute alcohol, and the solution of sodium ethylate cooled. Forty grams of ethyl acetoacetic ester were then added thru a reflux condenser, the solution again cooled, and twenty eight grams of benzyl chloride added thru a reflux condenser (one mole and five percent excess). The mixture was then heated upon the water bath with a reflux condenser until the dilution with water of a small portion no longer showed an alkaline reaction. The alcohol was then distilled off as far as possible, and the residue poured into water, shaken, separated, the dissolved ester removed with ether, the crude product dried over sodium sulfate, and distilled. There was no portion of the distillate which showed anything approaching a constant boiling point. The highest temperature reached during the distillation was two hundred sixty five degrees. Not over five cubic centimeters came thru the condenser between two hundred sixty and two hundred sixty five degrees. It was evident, of course, that ethyl benzyl ester had not been produced, or that it had decomposed under distillation.

In considering where the fault with this method of preparation might lie, it was reasoned as follows:

There were two hypotheses to reason from as to the cause of the results obtained, (1) and (2), as follows:

(1) When the crude product reached the distilling flask, there was no ethyl benzyl acetoacetic ester in the mixture. This seemed the most likely conclusion, since both Conrad-Limpach (1) and Dieckmann (2) had stated that ethyl benzyl acetoacetic ester is stable under atmospheric pressure. If this were true
as it seemed to be, then the most likely sources of error appeared to be the following:

(a) The alcohol used was a commercial absolute alcohol with no estimate of its purity upon the label. It gave a coloration with anhydrous copper sulfate in about three times the length of time that commercial ninety five percent alcohol did, hence, if there was an interference in the reaction by the effect of this small amount of water and sodium hydroxide formed from it upon treatment with sodium, a perfectly dry alcohol should show no interference with the formation of ethyl benzyl acetoacetic ester. In order to test this conclusion, very dry alcohol was prepared by treating "absolute" commercial alcohol with sodium (one-fifth mole sodium to one mole alcohol), distilling from a water bath, and rejecting the first and last one hundred cubic centimeters of the distillate. Three hundred cubic centimeters of pure alcohol were thus prepared.

In the manner previously described, eighty four grams of ethyl acetoacetate were treated with fourteen grams of sodium in two hundred cubic centimeters of alcohol, and with seventy grams of benzyl chloride (molar plus five percent excess); the preparation was then carried out essentially as before. The same result was obtained as in the previous attempt; nothing distilled over after two hundred sixty five degrees was registered on the thermometer immersed in the vapor.

(b) In distilling off the alcohol, in the attempts previously described, it was found necessary to place the flask containing the reaction mixture in an oil bath heated to one hundred twenty degrees in order to drive off the later portions of the alcohol. After this was done, a nauseous "cracked" odor was observed, quite unlike the characteristic acetoacetic ester.
This suggested that the ethyl benzyl acetoacetic ester had been formed, but had been decomposed by the continued heating with alcohol and the solid sodium chloride, which intensified the effect of the heat. This did not seem very likely, but in order to ascertain if this was the case, another attempt was made to prepare ethyl benzyl acetoacetic ester.

The procedure in this attempt follows:

One hundred and ten grams of ethyl acetoacetic ester were treated with eighteen grams sodium in two hundred fifty cubic centimeters of alcohol, and ninety two grams of benzyl chloride, as before, but when the reaction was complete as shown by the neutral reaction of the reaction mixture, the solid sodium chloride was filtered off on a Büchner funnel with suction, and repeatedly washed with dry ether until the washings showed no residue on evaporation of the ether from a portion. The washings were added to the original filtrate, and the ether-alcohol solution of the product distilled. Essentially the same result as in the previous attempts---no distillate with a boiling point of over two hundred sixty five degrees, was obtained.

(2). The negative results of these attempts suggested that ethyl benzyl acetoacetic ester was formed by all three of the above methods, but that Conrad-Limpach and Dieckmann had been wrong in stating that the ester boiled without decomposition under atmospheric pressure.

Another attempt was made to prepare ethyl benzyl acetoacetic ester using the procedure described above with one hundred and ten grams of ethyl acetoacetic ester, eighteen grams of sodium, ninety two grams of benzyl chloride and two hundred fifty cubic centimeters of alcohol, but after filtering off
the sodium chloride, the alcohol-ether solution was dried over sodium sulfate as before, and dropped from a dropping funnel into a Claisen flask on a water bath heated to eighty five degrees, and connected with a condenser cooled by water. When no further distillate was obtained, the residue in the flask was distilled under a pressure of fifty five millimeters of mercury. This time a constant boiling portion at one hundred ninety five to two hundred degrees was obtained, which was purified by two distillations under a pressure of fifty five millimeters as before. Yield-- seventy six grams, or about forty five percent. This fraction on distilling under atmospheric pressure, boiled at two hundred ninety seven to two hundred ninety nine degrees, corrected. The corrected boiling point as given by Conrad-Limpach, was two hundred ninety five to two hundred ninety eight degrees.

The distillates which were obtained in the first three attempts to prepare ethyl benzyl acetoacetic ester were now subjected to distillation under a pressure of fifty five millimeters. The fraction distilling between one hundred ninety and two hundred degrees weighed sixty grams.

Several preparations of ethyl benzyl acetoacetic ester were now made in the manner previously described; one of one hundred sixty grams with a yield of forty seven percent; another of one hundred and two grams, a yield of forty nine percent.

The next step in the synthesis was the saponification with sodium in alcohol (two percent) of the ethyl benzyl acetoacetic ester previously prepared, according to the method of Dieckmann (3). This was accomplished by the following procedure:

Seventy six grams of ethyl benzyl acetoacetic ester were
boiled for two hours with one and five tenths grams of sodium dissolved in seventy five cubic centimeters of absolute alcohol, the alcohol distilled off as far as possible, and the residue distilled. The portion with a boiling point of two hundred fifty one to two hundred fifty three degrees is the ethyl ester of ethyl benzyl acetic acid, also known as a-ethyl hydrocinnamic ethyl ester. The portion boiling from two hundred fifty one to two hundred fifty three degrees in this experiment weighed forty seven grams, a yield of about seventy five percent. The ethyl ester of the acid from the previous experiment weighing forty seven grams was now saponified with forty percent of sodium hydroxide, and the resulting acid after acidification distilled under reduced pressure with a yield of thirty nine grams, which is practically quantitative, except for losses in manipulation. In the same manner preparations of twenty five grams (from the distillates from the first three attempts to prepare ethyl benzyl acetoacetic ester), and seventy five grams were made with percentage yields which closely approached those given above. All of the above preparations boiled constant within plus or minus two degrees of two hundred seventy three degrees under atmospheric pressure, after being purified by distillation under diminished pressure, which agrees well with the boiling point of two hundred seventy two to two hundred seventy four degrees given by Baeyer and Jackson (4).

Nitration of ethyl benzyl acetic acid.

The acid was nitrated as follows:

Twenty cubic centimeters of fuming nitric acid were placed in a flask of fifty cubic centimeters capacity immersed in brine
and ice and the acid cooled to minus eight degrees; then drop by drop, five grams of ethyl benzyl acetic acid were added with constant stirring of the flask in the brine. The addition of the organic acid caused an immediate red coloration, which changed to an orange on continued shaking. The mixture, after the addition of all of the acid, was allowed to stand in the cooling mixture for forty five minutes, and then poured into finely crushed ice. The nitration product settled out as an oil and on thorough stirring gathered into a lump, of about the consistency of putty. The supernatant liquid was then decanted, and more ice added. The addition of ice and decantation of supernatant liquid was repeated at intervals during at least twenty four hours until the product finally assumed a crystalline appearance. It was then dissolved in ether, filtered, and petroleum ether added until the solution became opaque, when it was placed in a flask, stoppered, and allowed to crystallize. The crystals were not very pure, as their yellow color diminished on repeated recrystallization. In order to obtain a product with a constant melting point, seven recrystallizations were necessary. The melting point of the product thus purified was one hundred eighteen degrees.

A combustion was made to determine the percentage of nitrogen; the result was as follows:

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight of sample</td>
<td>0.2060 grams</td>
</tr>
<tr>
<td>Barometer temperature</td>
<td>23 degrees</td>
</tr>
<tr>
<td>Barometer reading</td>
<td>747.2 millimeters</td>
</tr>
<tr>
<td>Azotometer temperature</td>
<td>23 degrees</td>
</tr>
<tr>
<td>Volume of nitrogen</td>
<td>11.4 c.c.</td>
</tr>
<tr>
<td>Vapor pressure of 40% KOH at 23 degrees</td>
<td>11.1 millimeters</td>
</tr>
</tbody>
</table>

747.2 plus 11.1 mm=758.3 mm.---total pressure
Weight of one c.c. of N at 23 degrees and 758.3 mm.---1.118 milligrams.

Percentage of nitrogen in substance---- - -

\[
\frac{11.4}{0.206} \times \frac{(0.001118)}{(100)} = 6.19\% \text{ nitrogen}
\]

Calculated percent of nitrogen for

nitro-a-ethyl-hydrocinnamic acid-------- 6.29\% nitrogen

Difference---------------------------0.16\% of true N content.

To determine the position of the nitro group, one gram of the nitro-acid was oxidized with neutral permanganate solution, the reaction product filtered, the filtrate acidified, the solid nitrobenzoic acid recrystallized twice from alcohol, and a melting point taken.

The product melted at two hundred thirty three degrees (uncorrected). The melting point of para-nitrobenzoic acid, from Mulliken (5), is two hundred thirty four to two hundred thirty five degrees, uncorrected.

Para nitro-a-ethyl-hydrocinnamic acid is a white solid, when pure, insoluble in water and petroleum ether; soluble in nearly all organic solvents, such as ether, glacial acetic acid, alcohol, etc.

Preparation of para-amino-a-ethyl-hydrocinnamic acid hydrochloride:

Twenty grams of a-ethyl-hydrocinnamic acid were nitrated in five cubic centimeter portions, and the nitroacid freed of nitric acid as far as possible by the decantation mentioned above; weighed wet, the nitroacid weighed thirty five grams. This was transferred to a seven hundred fifty cubic centimeter
flask, and treated with tin and hydrochloric acid until the solid entirely dissolved. The tin was then removed from the solution by eight successive precipitations with hydrogen sulfide, the solution of the amine concentrated by evaporation, the amine hydrochloride crystallized and filtered, then recrystallized from alcohol as white needles. An attempt was made to determine the melting point of the amine, but it showed no signs of softening at three hundred twenty degrees, altho it was a carbon compound as shown by its smoky flame when burnt on platinum foil.

Preparation of the Racemic Dyestuff.

The racemic dyestuff was prepared from beta-napthol and p-a-ethyl hydrocinnamic acid diazonium chloride as follows:

Two grams of p-a-ethyl-hydrocinnamic diazonium chloride were placed in a beaker and dissolved in ten cubic centimeters of water; this was cooled in ice and salt and 0.3 cubic centimeters of hydrochloric acid (Specific Gravity 1.19) added. This was allowed to react while cooled in ice and salt. A solution of one and four tenths grams of beta napthol was prepared in an excess of twenty percent sodium hydroxide in another beaker and this also cooled.

The two solutions were next mixed thoroughly and allowed to stand for twenty four hours. Sample strips of cotton were then dyed in the solution of the sodium salt. The color dyed on cotton without the use of a mordant, is brown; when ferric alum is used as a mordant, a very dark green shade is imparted to the cloth.

Owing to lack of time, the experimental work was discontinued at this point.
III

CONCLUSION

It has been shown that ethyl benzyl acetoacetic ester is decomposed below its boiling point when present in a mixture under atmospheric pressure.

Para-nitro-a-ethyl-hydrocinnamic acid has been prepared and its constitution established.

Para-amino-a-ethyl-hydrocinnamic acid has been prepared, and a strong presumption established as regards its constitution.
B I B L I O G R A P H Y

(1) Ludwig Vanino --- Praparative Chemie, Organischer Teil; Seite 142, Zweiter Band.

(2) Berichte der Deutschen Chemischen Gesellschaft;
    Volume 11, Page 1057.

(3) Berichte der Deutschen Chemischen Gesellschaft;
    Volume 33, Page 2681

(4) Berichte der Deutschen Chemischen Gesellschaft;
    Volume 13, Page 118

(5) Mulliken---Identification of Organic Compounds
    Volume II.