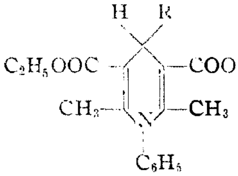
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

The Reactions of Aldehydes with β-Anilinocrotonic Esters[1]

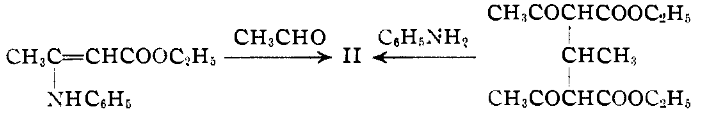
BY JOHN G. ERICKSON[2]

While Knoevenagel[3] has studied the reactions of benzaldehyde with some β-aminocrotonic esters, there appear to be no published studies of the reactions of aldehydes with β-anilinocrotonic esters alone. Lachowicz,[4] however, has reported that the reaction of benzaldehyde with a mixture of ethyl β-anilinocrotonate and ethyl acetoacetate yields 1,4-diphenyl-2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (I).



I, R = C_6H_5
II, R = CH_3

The present study deals with the reactions of acetaldehyde and benzaldehyde with β-anilinocrotonic esters. The reaction of acetaldehyde with ethyl β-anilinocrotonate was found to yield 1-phenyl-2,4,6-trimethyl-3,5-dicarbethoxy-1,4-dihydropyridine, II. The identity of II was proved by analysis and by mixed melting point determination with an authentic sample of II, prepared from aniline and ethyl ethylidene bis-acetoacetate.

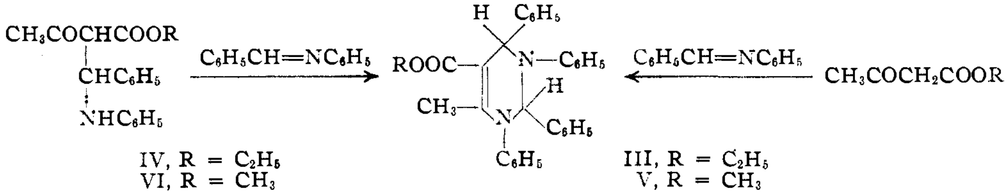


$$\underset{\displaystyle NHC_6H_5}{CH_3C}{=}CHCOOC_2H_5 \xrightarrow{CH_3CHO} II \xleftarrow{C_6H_5NH_2} \begin{array}{c} CH_3COCHCOOC_2H_5 \\ | \\ CHCH_3 \\ | \\ CH_3COCHCOOC_2H_5 \end{array}$$

From the reaction mixture of benzaldehyde with ethyl β-anilinocrotonate there were isolated two products, I and another compound (III), whose analysis corresponds most closely to the formula $C_{32}H_{30}N_2O_2$. Compound III has been prepared by Bertini,[5] who isolated it, as well as I, from the reaction mixture of benzalaniline with ethyl α-acetyl-β-anilinohydrocinnamate (IV). It has also been made by Philpott and Jones[6] by treatment of benzalaniline with ethyl acetoacetate. Bertini, on the basis of his analytical results, assigned III the structure of a tetrahydropyrimidine derivative.

On the basis of analytical results alone there are other formulas for III which are nearly as satisfactory as the molecular formula $C_{32}H_{30}N_2O_2$. Furthermore, plausible structures other than Bertini's can be written for the formula $C_{32}H_{30}N_2O_2$. Accordingly, additional work was carried out in order to establish the structure of III.

Benzaldehyde reacts with methyl β-anilinocrotonate, yielding a compound (V) whose analysis is consistent with the formula $C_{31}H_{28}N_2O_2$. Compound V can also be prepared by the action of benzalaniline on methyl acetoacetate or methyl α-acetyl-β-anilinohydrocinnamate (VI). Since Schiff and Bertini[7] have shown that ethyl acetoacetate reacts with benzalaniline to yield IV, it follows that the syntheses of Bertini and of Philpott and Jones are equivalent and that in the formation of III and V, the alpha carbon atom of the unsubstituted acetoacetic ester becomes attached to the anilinobenzyl grouping. It has been found that propyl acetoacetate reacts with benzalaniline to give a substance (VII) of molecular formula $C_{33}H_{32}N_2O_2$. Likewise, butyl acetoacetate reacts with benzalaniline to give a substance similar to III, V and VII. It is apparent that, since the reactions of benzalaniline with each of four alkyl acetoacetates give four similar but different products, the ester grouping must be left intact in each of these reactions and all of the oxygen present in III, V and VII must be contained in carboalkoxy groupings. Furthermore, attachment of the beta carbon atoms to nitrogen atoms is indicated. The validity of this latter statement is based upon the fact that ethyl and methyl β-anilinocrotonates react with benzalaniline to yield III and V, respectively.



IV, R = C_2H_5
VI, R = CH_3

III, R = C_2H_5
V, R = CH_3
VII, R = n-C_3H_7

It was not found possible to cause ethyl α-methylacetoacetate to react with benzalaniline. A not unreasonable conclusion from this result is that in the formation of III, V and VII, the gamma carbon atoms of the acetoacetic or β-anilinocrotonic esters are not involved. It follows

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[1] Abstracted from the Ph.D. thesis of John G. Erickson, May, 1944.

[2] Present address, American Cyanamid Company, Stamford, Conn.

[3] Knoevenagel, *Ber.*, **31**, 738–748 (1898).

[4] Lachowicz, *Monatsh.*, **17**, 343–360 (1896).

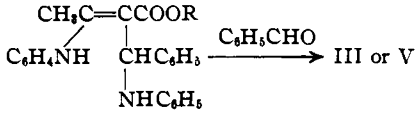
[5] Bertini, *Gazz. chim. ital.*, **29**, 11, 30–35 (1899).

[6] Philpott and Jones, *J. Chem. Soc.*, 337–341 (1938).

[7] Schiff and Bertini, *Ber.*, **30**, 601–604 (1897).

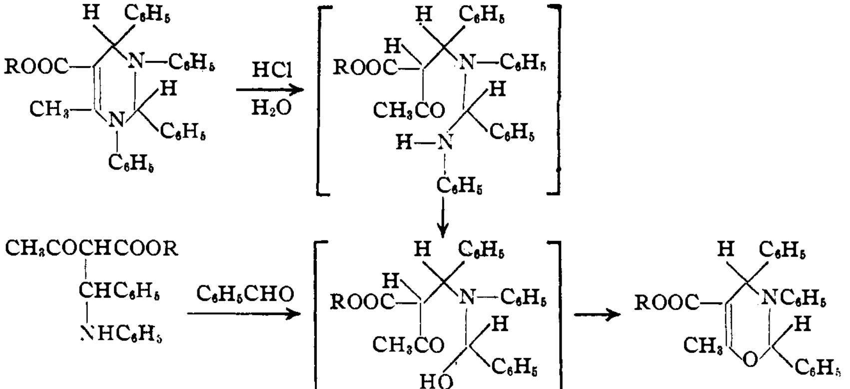
from these considerations that the most likely structure for III is the one proposed by Bertini and that V and VII have analogous structures.

The synthesis of III and V was attempted, using the reaction of benzaldehyde with ethyl and methyl α-(α-anilinobenzyl)-β-anilinocrotonates (VIII and IX)


VIII, R = C_2H_5
IX, R = CH_3

Two syntheses of VIII and IX presented themselves. However, one, the reaction of benzalaniline with β-anilinocrotonic esters, gave only III or V, whether one or two moles of benzalaniline were used. The second proposed synthesis of VIII and IX involved the action of aniline on IV and VI. Treatment of IV and VI with aniline gave viscous oils which could not be crystallized but which, in the case of the methyl ester only, on treatment with benzaldehyde gave a good yield of the desired product.

The chemical nature of III (and V) is of some interest. Bertini stated that III is chemically very resistant. The present work has indicated that this statement should be modified. Heated at 250° III rapidly yields a small amount of *s*-diphenylurea, besides much resinous material. Two moles of methane are slowly formed when III or V is treated with methylmagnesium iodide, but there is no evidence of any addition reaction occurring during this treatment.


XI, R = C_2H_5
XII, R = CH_3

Compound III slowly dissolves in hot glacial acetic acid to form a compound (X), m. p. 237–238°, whose analysis is most consistent with the formula $C_{24}H_{23}NO_2$. Since similar treatment of V gives a compound, m. p. 249–254°, it would appear that in X the carbethoxy grouping has been retained. Compound X is quite resistant to the action of acids and bases. There is insufficient evidence to warrant suggesting a structure for X.

While III and V are stable toward bases, they are quite sensitive toward acids. The action of a mixture of dioxane and aqueous hydrochloric acid upon III and V yields $C_{26}H_{25}NO_3$ (XI) and $C_{25}H_{23}NO_3$ (XII), respectively. The formation of these compounds is viewed as occurring by way of hydrolysis of the vinylamine groupings in III and V, followed by replacement of the resulting anilino groups by hydroxyl groups and subsequent recyclization.

This formulation of XI and XII is supported by syntheses which, although they yielded insufficient material for complete purification, leave little room for doubt as to the structures of XI and XII. Compounds IV and VI, treated with benzaldehyde, yield small amounts of XI and XII. These latter reactions are analogous to the synthesis by Betti[8] of a naphthoxazine from benzaldehyde and β-(α-anilinobenzyl)-α-naphthol. It might be objected that XI and XII, obtained in this way from IV and VI, might actually be the products of acid degradation of III and V, these latter compounds being formed from IV and VI and benzalaniline resulting from decomposition of part of the IV and VI. This possibility seems unlikely since the small amounts of XI and XII this synthesis does afford are formed rapidly and prolonged standing does not improve the yield except after days.

The use of stronger acid and shorter reaction periods converts III into an unstable material (XIII), m. p. 118–120.5°, instead of XI. Compound XIII, treated with pyridine or a mixture of dioxane and aqueous hydrochloric acid, is converted into XI. The action of ethanolic sodium hydroxide upon XIII appears to convert it into a still more labile compound which, refluxed briefly with alcohol after acidification with acetic acid, yields XI. No product analogous to XIII could be isolated from reaction mixtures of V and acids of various concentrations.

I am deeply indebted to Dr. W. M. Lauer for assistance in the performance of this research. I also wish to thank Messrs. Chien-Pen Lo and Vincent Webers for performing several of the analyses reported in this paper.

Experimental[9]

The Reaction of Ethyl β-Anilinocrotonate with Acetaldehyde.—Twenty grams (0.0975 mole) of ethyl β-anilino-

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[8] Betti, *Gazz. chim. ital.*, **31**, 377 (1901).

[9] All melting points are corrected values.

crotonate and 4.3 g. (0.0975 mole) of freshly distilled acetaldehyde were mixed, the mixture cooled in an ice-bath and two drops of concentrated hydrochloric acid added to this mixture. Within five minutes the mixture became cloudy. The mixture was then allowed to stand at room temperature. After six days a considerable amount of water had separated from the mixture. Removal of the water by the use of a vacuum desiccator left a dark viscous oil. Forty cubic centimeters of 95% ethanol was added and an attempt was made to crystallize the reaction mixture. This attempt failing, the mixture was put aside.

After several months it was noticed that crystals had begun to form in the alcoholic solution of the reaction mixture. After nineteen months the mixture had become transformed into a number of large rhombic crystals covered by a dark viscous oil which was only slightly soluble in alcohol. The crystals were picked out and washed with dilute ethanol. The product from this treatment weighed 1.12 g. and melted at 100–105°. Three recrystallizations from dilute ethanol gave long white needles, m. p. 104–105°.

Anal. Calcd. for $C_{20}H_{25}NO_4$: C, 69.94; H, 7.34; N, 4.08. Found: C, 70.32; H, 7.33; N, 4.17.

1-Phenyl-2,4,6-trimethyl-3,5-dicarbethoxy-1,4-dihydropyridine.—Ethyl ethylidene bisacetoacetate was prepared following the directions of Rabe and Elze.[10] The ester (8.58 g., 0.030 mole) was dissolved in 10 cc. of 95% ethanol. To this solution were added 2.8 g. (0.030 mole) of aniline and four drops of concentrated hydrochloric acid.

After forty-eight hours large rhombic crystals had appeared in the solution; disturbance of the solution caused smaller crystals to appear. After five days, 5 cc. of water was added to the solution and the mixture was cooled to 5° and maintained at this temperature for sixteen hours. The mixture was then filtered and the precipitate washed with a few cc. of dilute (1:1) ethanol. Pressing the product on a porous plate gave 2.75 g. of material melting at 95–102°. Recrystallization from dilute ethanol gave 2.42 g. (23.8% yield) of white needles, m. p. 104–105°. Admixture with the reaction product of ethyl β-anilinocrotonate and acetaldehyde resulted in no depression of the melting point.

Reaction of Ethyl β-Anilinocrotonate with Benzaldehyde.—Forty-one grams (0.20 mole) of ethyl β-anilinocrotonate and 21.2 g. (0.20 mole) of benzaldehyde were mixed and three drops of concentrated hydrochloric acid added to the mixture. A small amount of white solid, presumably the hydrochloride of the amino ester, separated immediately. After several minutes the mixture became cloudy and the white solid redissolved in the mixture. The temperature of the mixture rose from 25 to 47.5° within ten minutes of mixing. After fifteen minutes the mixture was very cloudy and quite viscous. After five days the supernatant water layer was removed and the viscous oil was dissolved, with warming, in 200 cc. of 95% ethanol.

Within a very few minutes a precipitate had begun to form. After four days the mixture was filtered and the precipitate was washed with 50 cc. of 95% ethanol. The weight of the light yellow material obtained in this manner was 20.8 g. The combined filtrate and washings, after standing forty-eight hours longer, deposited a further 0.30 g. The product thus obtained melted at 130–140°.

The alcoholic mother liquor was poured into 300 cc. of water. After the brown oil had separated completely, the water was poured off and the oil was dried under reduced pressure and recrystallized from benzene and petroleum ether. This procedure yielded a yellow material which was recrystallized twice from 95% ethanol. There was obtained 0.85 g. of a solid possessing a faint greenish-yellow tinge, m. p. 156–158°. Admixture with an authentic sample of 1,4-diphenyl-2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine[4] resulted in no depression of the melting point.

The yellow precipitate isolated above by virtue of its slight solubility in cold alcohol is not easily purified. The best method of purification appears to be to dissolve the material in the minimum amount of hot benzene and then to reprecipitate the product by the addition of several volumes of 95% ethanol, followed by cooling. After several applications of this procedure the product is colorless and melts at about 150–155°. It is then recrystallized from 1:4 benzene–ethanol and finally from 95% ethanol, in which it is only slightly soluble. Crystallization from alcohol gives small rhombic crystals, melting at 175–176°, which are stable in air. Crystallization from benzene or xylene gives much larger crystals which, however, crumble on exposure to air.

Anal. Calcd. for $C_{32}H_{30}N_2O_2$: C, 80.98; H, 6.37; N, 5.90; mol. wt., 474.6. Found: C, 80.75, 81.31; H, 6.09, 6.15; N, 6.00; mol. wt., 457, 468 (benzene f. p.).

Admixture of this product with samples of 1,2,3,4-tetraphenyl-5-carbethoxy-6-methyl-1,2,3,4-tetrahydropyrimidine, prepared by the procedures of Bertini or of Philpott and Jones or by the following syntheses, did not produce a depression of the melting point.

Syntheses of $C_{32}H_{30}N_2O_2$: (a) From Ethyl Acetoacetate, Benzaldehyde and Aniline.—Sixty-four grams (0.603 mole) of benzaldehyde, 56.2 g. (0.604 mole) of aniline and 39.0 g. (0.302 mole) of ethyl acetoacetate were mixed and the mixture was dissolved in 100 cc. of 95% ethanol. Three drops of concentrated hydrochloric acid was then added. An insoluble oil separated from the solution after two hours. After standing for two weeks, this oil had changed to a light yellow solid. The mixture was then filtered. The product, after one recrystallization from benzene, weighed 82.3 g. and melted at 137–153°. Two further recrystallizations from benzene yielded 24.0 g. of product, m. p. 168–172°.

(b) **From Ethyl β-Anilinocrotonate, Benzaldehyde and Aniline.**—Sixty-two grams (0.30 mole) of ethyl β-anilinocrotonate, 64.0 g. (0.60 mole) of benzaldehyde and 28.2 g. (0.30 mole) of aniline were mixed and the mixture then dissolved in 100 cc. of 95% ethanol. Four drops of concentrated hydrochloric acid was added to the mixture which was then allowed to stand for nine days. The mixture was filtered and the precipitate, a light yellow solid, was washed with ethanol. The weight of dry crude product, m. p. 135–145°, was 130.0 g. This corresponds to a 91% yield of the crude product.

(c) **From Ethyl β-Anilinocrotonate and Benzalaniline.**—Ethyl β-anilinocrotonate (2.05 g., 0.01 mole) was mixed with 3.62 g. (0.02 mole) of benzalaniline and 0.5 g. of Drierite. Approximately 1 mg. of aniline hydrochloride was added to the mixture which was then heated on the steam cone for forty-eight hours. At the end of this period the viscous liquid, while still hot, was separated by decantation from the Drierite. The Drierite and flask were then washed with a mixture of 5 cc. of ethyl ether and 30 cc. of ethanol. Upon addition of these washings to the main body of the product, crystallization started immediately. The mixture was filtered after fifteen minutes. The weight of dry, light yellow product, m. p. 160–165°, was 2.0 g. After recrystallization from ethanol the product melted at 172–173°.

(d) *Via* **Ethyl α-(α-Anilinobenzyl)-β-anilinocrotonate.**—Ethyl α-acetyl-β-anilinohydrocinnamate[7] (0.93 g., 0.003 mole) and aniline (0.28 g., 0.003 mole) were mixed and dissolved in 3 cc. of benzene. After less than one hour the solution had become cloudy. After twenty-four hours a considerable amount of water had formed. The benzene and water were removed by evaporation under reduced pressure at room temperature. There remained a rather viscous yellow oil, soluble in benzene, alcohol and ether. Attempts to cause this oil to crystallize failing, the oil was dissolved in 3 cc. of benzene and to this solution was added 0.32 g. (0.003 mole) of benzaldehyde. The solution became cloudy within one minute. After several hours, the benzene and water were removed by the use of reduced pressure and 5 cc. of ethanol was added to the viscous residue. A precipitate began to form in a few minutes. The mixture was filtered after two hours. The weight of dry crude product, melting at about 160°, was 0.05 g.

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(10) Rabe and Elze, *Ann.*, **323**, 99 (1902).

Recrystallized from ethanol, the product melted at 172–173°.

Reaction of Methyl β-Anilinocrotonate with Benzaldehyde.—Methyl β-anilinocrotonate (47.8 g., 0.25 mole) and 23.3 g. (0.25 mole) of benzaldehyde were mixed. There was a definite cooling effect attending this mixing, the temperature of the mixture dropping to about seven degrees below room temperature. The mixture was then warmed gently on the steam cone in order to achieve homogeneity and five drops of concentrated hydrochloric acid added to the mixture.

In a very few minutes the mixture became quite turbid but never very warm. After several days the mixture had become a very viscous oil covered by a layer of water. The water was removed and 150 cc. of methanol was added to the oil. A few minutes of gentle warming on the steam cone caused the oil to dissolve in the methanol. This solution then rapidly precipitated a nearly white solid. The solid was filtered off after several hours and washed with a small amount of methanol. The yield of crude dry product obtained in this manner was 30.6 g.

The purification of this product is accomplished in very much the same fashion as is that of III except that methanol is used in place of ethanol in the procedure previously described. The purification of V was found, however, to be more easily achieved than that of III. Final recrystallization from methanol or from benzene–methanol gives long white needles, m. p. 192–193°.

Anal. Calcd. for $C_{31}H_{28}N_2O_2$: C, 80.94; H, 6.00; N, 6.09; mol. wt., 460.6. Found: C, 81.14, 81.28; H, 5.62, 6.32; N, 6.23; mol. wt. (benzene f. p.), 416.

Admixture of this product with samples of 1,2,3,4-tetraphenyl - 5 - carbomethoxy - 6 - methyl - 1,2,3,4 - tetrahydropyrimidine, prepared by any of the following syntheses, did not produce a depression of the melting point.

Syntheses of $C_{31}H_{28}N_2O_2$: (a) From Methyl α-Acetyl-β-anilinohydrocinnamate.—Methyl α-benzalacetoacetate was prepared, following the direction of Knoevenagel.[11] It is a light yellow liquid, boiling at 158–162° under 12 mm. of pressure. Following the procedure of Ruhemann and Watson,[12] the benzalacetoacetic ester was converted in good yield into methyl α-acetyl-β-anilinohydrocinnamate. This latter compound is a white solid, melting, with rapid heating, at 119–122°. It may also be obtained from the reaction of methyl acetoacetate with benzalaniline.

Methyl α-acetyl-β-anilinohydrocinnamate (0.30 g., 0.001 mole) was mixed with 0.18 g. (0.001 mole) of benzalaniline. Three grams of benzene and about 1 mg. of aniline hydrochloride were then added. After eight days the solvent was removed under reduced pressure at room temperature. Four grams of methanol was then added. Crystallization of the product proceeded fairly rapidly. The weight of the dry crude product, filtered off after twenty-five hours, was 0.07 g. After recrystallization from methanol–benzene the product melted at 187–190°.

(b) **From Methyl β-Anilinocrotonate and Benzalaniline.**—This was done in a manner similar to that used with the ethyl ester. Equivalent quantities and the same conditions were employed. The yield of crude dry product was 2.10 g. Recrystallized from methanol–benzene, it melted at 191–193°.

(c) ***Via* Methyl α-(α-Anilinobenzyl)-β-anilinocrotonate.**—This was done in a manner exactly analogous to that employed with the ethyl ester, eqiuivalent quantities being used. There was obtained 0.61 g. of crude product. After three recrystallizations from methanol–benzene, the product melted at 188–192°. Efforts to repeat this experiment were never successful.

Reaction of *n*-Propyl Acetoacetate with Benzalaniline.—Propyl acetoacetate (1.44 g., 0.010 mole) was mixed with 3.62 g. (0.020 mole) of benzalaniline and the mixture was then melted by gentle heating. Approximately 1 mg. of aniline hydrochloride was added. After forty-eight hours at room temperature the mixture was a jelly-like mass. It was dissolved, with warming, in 15 cc. of *n*-propanol. After nine days the formation of precipitate had apparently ceased. The precipitate was filtered off and recrystallized three times from *n*-propanol; 2.29 g. of product, m. p. 146–147°, was obtained.

Anal. Calcd. for $C_{33}H_{32}N_2O_2$: C, 81.12; H, 6.60; N, 5.74. Found: C, 81.39; H, 6.50; N, 5.72.

Conversion of III into XI.—Ten grams of III was dissolved in 700 cc. of dioxane. To this solution were added 80 cc. of water and 80 cc. of concentrated hydrochloric acid. The solution immediately became colored a bright greenish-yellow upon addition of the acid. After standing twenty-eight hours at room temperature, the solution, now colored a greenish-brown, was poured into 4 liters of water. After another twenty-eight hours, the suspension resulting from this treatment was filtered. One recrystallization of the oily precipitate from ethanol gave 2.65 g. of pink needles, m. p. 148–152°.

The removal of the pink color is a matter of some difficulty as this color is strongly absorbed from solution by the crystals of XI and is apparently not absorbed at all by charcoal. Removal of the color was accomplished by dissolving the pink needles in more than the minimum amount of hot alcohol, allowing the product to crystallize by cooling, removing these crystals by filtration and then concentrating the filtrate under reduced pressure. The material, thus obtained from the filtrate, is, after another recrystallization from ethanol, very nearly white and melts at 148–150° with some softening at about 143°.

Anal. Calcd. for $C_{26}H_{25}NO_3$: C, 78.17; H, 6.31; N, 3.51. Found: C, 78.25; H, 6.35; N, 3.61.

Synthesis of XI.—Ethyl α-acetyl-β-anilinohydrocinnamate (0.31 g., 0.001 mole) and 0.11 g. (0.001 mole) of benzaldehyde were mixed and the mixture dissolved with gentle warming in 2 cc. of ethanol. One drop of glacial acetic acid was then added, the solution was warmed a few minutes longer and was then allowed to stand for an hour. Several cubic centimeters of water was then added. An oil separated which, after several recrystallizations from ethanol, gave a small amount of pinkish-white crystals melting at 126–130°. There was insufficient material for further purification. A mixture of this product with XI, prepared by degradation of III, melted at 144–149°.

Conversion of III into XIII.—Ten grams of III was dissolved in a mixture of 100 cc. of dioxane, 15 cc. of water and 25 cc. of concentrated hydrochloric acid. After standing two and one-half hours at room temperature, the yellow solution was poured into 850 cc. of water. After standing for twenty-four hours at room temperature, the suspension thus obtained had deposited a considerable amount of yellow nodules. These were filtered off and recrystallized from ethanol. Two such recrystallizations gave 6.90 g. of white needles, m. p. 116–119°. Three more recrystallizations from ethanol raised the melting point to 118–120.5°. The material is apparently unstable and the amount of heating to which alcoholic solutions are subjected during recrystallization appears to affect the melting point.

Anal. Found: C, 78.51; H, 6.49; N, 3.82.

Conversion of III into X.—Five and six-tenths grams of III was warmed with 40 cc. of glacial acetic acid on the steam cone until solution was complete. This process required about fifteen minutes. At this stage the solution was dark red. Water was then added dropwise until the turbidity persisted and the mixture was allowed to cool. After twenty-four hours a precipitate had appeared and was filtered off. The filtrate was warmed and to it was added more water. After a second period of twenty-four hours another crop of solid had appeared and was filtered off and added to the first crop. The combined product was recrystallized twice from dilute ethanol. This treatment gave 0.9 g. of white flakes, m. p. 237–238°.

Anal. Calcd. for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92. Found: C, 80.52; H, 6.50; N, 4.10.

Pyrolysis of III.—This was accomplished by placing the sample of III, contained in an Erlenmeyer flask, in a fusible alloy bath, preheated to 250°. Within five minutes of

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(11) Knoevenagel, *Ber.*, **29**, 172 (1896).

(12) Ruhemann and Watson, *J. Chem. Soc.*, **85**, 1170 (1904).

heating, some material had appeared on the cooler parts of the flask. Further heating had no effect. The sublimate was then scraped from the walls of the flask and recrystallized from ethanol. Only a few milligrams of product melting at 236–237° was obtained for each gram of III used. Admixture with an authentic sample of *s*-diphenylurea produced no depression of the melting point.

Conversion of V into XII.—Two grams of V was dissolved in 125 cc. of dioxane and 10 cc. of water and 10 cc. of concentrated hydrochloric was then added. There was immediate formation of a yellow color upon addition of the acid. After standing for twenty-four hours, the solution was poured into 300 cc. of water.

After standing for forty-eight hours, the suspension resulting from this treatment had deposited yellow leaves. These were removed by filtration and washed with water. There was obtained in this manner 0.70 g. of dry yellow product, m. p. 166–176°. Two recrystallizations from methanol gave pink needles melting at 175–177°.

The pink color accompanying this product is as difficult to remove as that accompanying XI; its removal was accomplished by use of the same technique as that previously described for XI. This treatment gave very nearly white needles, m. p. 177–178°.

Anal. Calcd. for $C_{25}H_{23}NO_3$: C, 77.90; H, 6.01; N, 3.63. Found: C, 78.00; H, 6.74; N, 3.74.

Synthesis of XII.—Four-tenths gram of methyl α-acetyl-β-anilinohydrocinnamate and 0.50 g. of benzaldehyde were mixed and dissolved in 1 cc. of methanol with warming. One drop of concentrated sulfuric acid was added and the solution warmed for a few minutes longer, then allowed to cool. After two hours a small amount of precipitate had appeared. This was filtered off and recrystallized from dilute methanol; there was not enough material for two recrystallizations. There was obtained a white powder, m. p. 148–157°; admixture with XII gave a melting point of 152–164°.

Summary

1. It has been shown that the reaction of acetaldehyde with ethyl β-anilinocrotonate yields a dihydropyridine derivative.

2. It has been shown that the reaction of benzaldehyde with ethyl β-anilinocrotonate yields a dihydropyridine derivative and a tetrahydropyrimidine derivative and that the reaction of benzaldehyde with methyl β-anilinocrotonate yields a tetrahydropyrimidine derivative.

3. Several degradation products of these tetrahydropyrimidines have been isolated. The action of dilute hydrochloric acid upon these tetrahydropyrimidines yields compounds which are probably oxazines.

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[CONTRIBUTION FROM THE DIVISION OF PHYSIOLOGICAL CHEMISTRY, UNIVERSITY OF MINNESOTA, MINNEAPOLIS]

Spectrophotometric Studies of the Oxidation of Fats. II. The Oxidation of Dienoic Fatty Acids

BY RALPH T. HOLMAN,[1] WALTER O. LUNDBERG[2] AND GEORGE O. BURR

The changes in fats which take place during autoxidation have been the subject of much study and many workers have proposed mechanisms for the oxidation of the component unsaturated fatty acids. Von Mikusch and Priest[3] have summarized briefly the theories and proposed mechanisms by which oxygen may attack the double bond. The mechanism whereby a four-membered ring peroxide is formed is favored with the more unsaturated fatty acids. The demonstration of oxido structures among the products of autoxidation of monoethylenic systems by Ellis[4] and Deatherage and Mattill[5] lends support to the mechanism leading to a three-membered ring peroxide containing tetravalent oxygen. Fahrion[6] first proposed a rearrangement of peroxides to form a ketol and Morrell[7] and co-workers have been able to identify ketols as products of oxidation of β-eleostearin.

Ellis[8] suggested that the addition of oxygen to the double bond yields an ene-diol. Scheiber[9] postulated the addition of oxygen to the unconjugated diene system at the active methylene group to form —CH=CH—CO—CH=CH—. Farmer[10,11] proposed a mechanism whereby oxygen attacks the carbon between the double bonds of the linoleic acid type system to yield a hydroperoxide. It will be noted that in the last three mechanisms the system retains its unsaturation after the addition of oxygen. In disagreement with these mechanisms is the work of Paschke and Wheeler[12] who found the decrease in iodine value roughly parallel to the increase in peroxide value during the oxidation of fatty acid esters.

Some work has been done relative to the spectroscopy of fat oxidations. Edisbury and co-workers[13] found an increase in the absorption of ling oil upon its exposure to air. In the oxidized sample there was an indication of an absorp-

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(2) Present address: Hormel Institute, Austin, Minnesota.

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