extraction of the diphenyl ether mother liquor with dilute alkali. The solid product weighed 0.7 g. (44%) and melted at 199–201° after recrystallization from methanol. Bobranski reported that 4-hydroxyquinoline melted at 201°.[14]

Ethyl α-Methyl-β-m-chloroanilinoacrylate.—To 255.2 g. (2.0 moles) of *m*-chloroaniline in 1200 cc. of water containing 166.8 cc. (2.0 moles) of concentrated hydrochloric acid (sp. gr. 1.187) was added 50 cc. (0.6 mole) of concentrated hydrochloric acid. The solution was stirred and the aqueous solution of ethyl α-sodioformylpropionate from 5.0 moles of ester was added dropwise over a three-hour period. During the same period, 367 cc. (4.4 moles) of concentrated hydrochloric acid was added. Light yellow solid appeared very soon after the first drops had been added, and stirring was continued for one hour. The solid acrylate was isolated by filtration, and washed once with water. The major part of occluded *m*-chloroaniline was removed by washing with 500 cc. of petroleum ether (b. p. 90–110°) and filtration. After thorough drying, 261.7 g. (21.9%) of ethyl α-methyl-β-*m*-chloroanilinoacrylate, m. p. 93–96°, was obtained as long shiny white needles. The ester was not completely stable and decomposed when dried at 65°. It turned slightly yellow when dried over phosphorus pentoxide at room temperature for two days.

Anal. Calcd. for $C_{12}H_{14}ClNO_2$: C, 60.13; H, 5.89. Found: C, 59.57; H, 5.93.

Methyl α-Methyl-β-m-chloroanilinoacrylate.—The methyl ester was prepared by the same method outlined above in which methyl propionate was condensed with ethyl or methyl formate to produce methyl α-sodioformylpropionate. The methyl α-methyl-β-*m*-chloroanilinoacrylate melted at 113.5–115.5°.

Anal. Calcd. for $C_{11}H_{12}ClNO_2$: C, 58.54; H, 5.36. Found: C, 58.73; H, 5.55.

7-Chloro-4-hydroxy-3-methylquinoline.—Ten grams (0.445 mole) of methyl α-methyl-β-*m*-chloroanilinoacrylate was boiled for twenty minutes in 30 cc. of Dowtherm. The solid product weighed 7.3 g. (85%), m. p. 255–312°. On recrystallization from ethanol, 65 to 75% of the crude material was recovered as white needles of 7-chloro-4-hydroxy-3-methylquinoline, m. p. 334–337°.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16. Found: C, 62.08; H, 4.17.

5-Chloro-4-hydroxy-3-methylquinoline.—The isolation of the isomeric quinoline from the cyclization of methyl or ethyl β-*m*-chloroanilinomethacrylate was accomplished by recrystallization from acetic acid. From 4.8 g. of crude cyclization product dissolved in 50 cc. of hot glacial acid, 2.1 g. of the 7-chloro isomer was obtained upon cooling. Addition of 50 cc. of water to the heated filtrate produced 0.9 g. of a mixture, chiefly of the 7-chloro isomer. Addition of 200 cc. of water to the hot filtrate in turn yielded 1.4 g. of product, m. p. 215–220°. Numerous recrystallizations of this material from ethanol gave white needles of 5-chloro-4-hydroxy-3-methylquinoline, m. p. 268–269.5°.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; N, 7.23. Found: C, 61.89; H, 4.20; N, 7.33.

7-Chloro-4-hydroxy-2-methylquinoline.—The general method of Limpach[15] was utilized to prepare this quinoline. Twenty-six grams (0.2 mole) of acetoacetic ester and 25.5 g. (0.2 mole) of *m*-chloroaniline were mixed and allowed to stand at room temperature overnight. No water layer had formed so two drops of concentrated hydrochloric acid were added. Within five minutes a definite lower layer of water appeared. After standing five hours the water layer was removed and the organic layer was dried over magnesium sulfate. To 200 cc. of refluxing Dowtherm was added 20 g. (0.084 mole) of the oily crotonate. Heating was continued for one-half hour. The product which precipitated from the cooled Dowtherm weighed 11.6 g. (72%). After three recrystallizations from dilute ethanol, 7-chloro-4-hydroxy-2-methylquinoline melted at 313.5–315°.

Anal. Calcd. for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; N, 7.23. Found: C, 62.31; H, 4.37; N, 7.41.

This compound is not identical with the high-melting product from the cyclization of the *m*-chloroanilinoacrylate, which was not appreciably soluble in warm ethanol or methanol and melted at a much higher temperature (390°).

Summary

Methyl β-anilinoacrylate has been cyclized to 4-hydroxyquinoline by heating at high dilution in boiling diphenyl ether solution. The *m*-chloroanilinoacrylate and methacrylate gave mixtures of 5- and 7-chloro-4-hydroxyquinoline and its 3-methyl homolog, respectively.

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[14] Bobranski, *Ber.*, **69**, 1113 (1936).

[15] Limpach, *ibid.*, **64**, 969 (1931).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Experiments on the Synthesis of 4-Hydroxy- and 4-Chloroquinolines from β-Anilinopropionic Acids[1]

BY ROBERT C. ELDERFIELD, WALTER J. GENSLER, THOMAS H. BEMBRY, CHESTER B. KREMER, FREDERICK BRODY, HOWARD A. HAGEMAN AND JAMES D. HEAD

The observation of Clemo and Perkin,[2,3] that certain β-anilinopropionic acids as their N-*p*-toluenesulfonyl (tosyl) derivatives undergo ring closure to dihydro-4-quinolone derivatives when treated with phosphorus pentoxide suggests the possibility that these acids might serve as a convenient source of 4-hydroxyquinolines and 4-chloroquinolines, the latter having assumed importance as intermediates in the synthesis of the members of the highly active 4-aminoquinoline group of antimalarial drugs. Clemo and Perkin also reported the formation of 1-tosyl-3-chlorodihydroquinolones when the anilinopropionic acid derivatives were subjected to the action of phosphorus oxychloride. Backeberg[4] reinterpreted the experimental observations of Clemo and Perkin on the latter reaction and showed that the product of the ring closure of N-tosyl-β-anilino-

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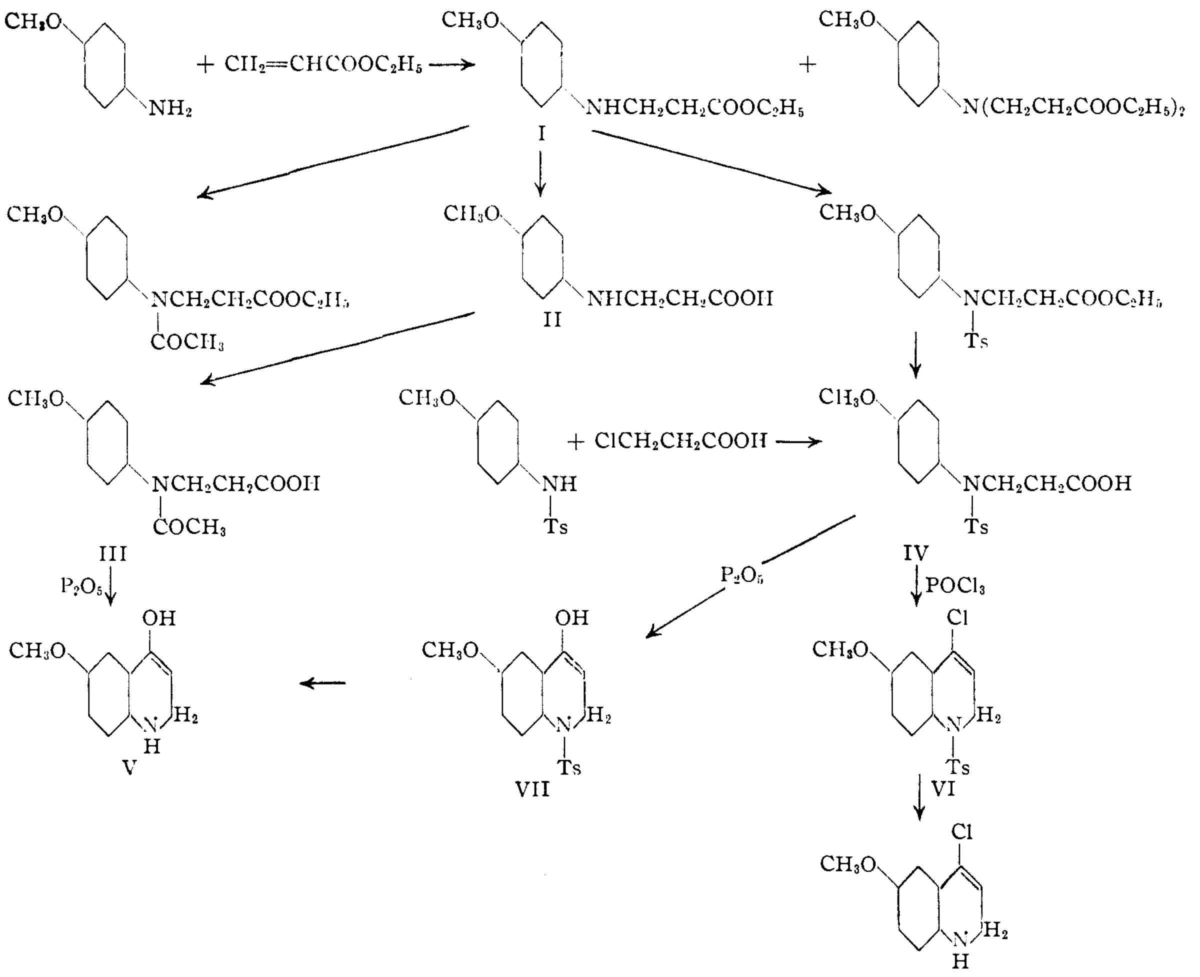
[1] The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University.

[2] Clemo and Perkin, *J. Chem. Soc.*, **125**, 1608 (1924).

[3] Clemo and Perkin, *ibid.*, **127**, 2297 (1925).

[4] Backeberg, *ibid.*, 618 (1933).



propionic acid with phosphorus oxychloride was in reality 1-tosyl-4-chloro-1,2-dihydroquinoline from which a small amount of 4-chloroquinoline could be obtained on oxidation.

A reinvestigation of this synthesis of 4-chloroquinolines was undertaken, since β-anilinopropionic acids are at present potentially readily available by addition of an aromatic amine to either ethyl acrylate or acrylonitrile. It soon became apparent that the reactions involved are somewhat obscure. At this time we wish to present the results of a preliminary study of the synthesis, since recent events have necessitated abandonment of the work by several of us.

p-Anisidine does not add to ethyl acrylate under the influence of basic catalysts which usually promote addition of alkylamines to such double bonds. However, in the presence of acetic acid[5] a good yield of ethyl β-anisidinopropionate (I) is obtained along with smaller amounts of anisidine-N,N-(di-β-propionic ester) and two unidentified other products. I is somewhat unstable, particularly when subjected to the action of heat or to acid, under the influence of which the addition reaction reverses. Hydrolysis of I under carefully controlled conditions resulted in the formation of β-anisidinopropionic acid (II). As usually obtained, this melted at 87–88°. However, in one experiment the acid was obtained melting at 76–77° and giving a satisfactory neutralization equivalent. No explanation for this is at hand beyond the possibility that it may have been an unstable isomorph. More obscure was the formation of substance melting at 74–75° and giving a neutralization equivalent of 410 and analytical figures not agreeing with the expected values when the ester was hydrolyzed with 40% alkali. This material apparently was closely related to II, since on acetylation the same acetyl derivative was obtained from it as was obtained from II. An acid giving an abnormally high molecular weight has been reported by Clemo and Perkin[2] from the action of β-chloropropionic acid on tosyl anilide. Like the compound encountered by us, the latter also is apparently closely related to the expected product of the reaction, N-tosyl-β-anilinopropionic acid, since both gave the same methyl ester. The nature of our substance was not investigated further at this time.

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(5) We wish to acknowledge our indebtedness to Dr. H. A. Bruson of Resinous Chemicals, Inc., for the suggested use of acetic acid as catalyst.

p-Anisidine also adds to acrylonitrile to yield β-(*p*-anisidino)-propionitrile; however, the yield of the propionic acid obtained on hydrolysis of the nitrile was so low that this approach was not investigated further.

m-Chloroaniline also gave ethyl β-(*m*-chloroanilino)-propionate when added to ethyl acrylate. Both the tosyl ester and acid failed to crystallize.

Ring closure of II to a 4-hydroxy- or 4-chloro-1,2-dihydroquinoline under a variety of reagents and conditions resulted only in the formation of unstable or intractable oils or tars. It appears as though protection of the free hydrogen on the nitrogen is a necessary condition for the isolation of well-defined products of ring closure. Accordingly, the preparation of several N-substituted derivatives of II in addition to the derivative of Clemo and Perkin was undertaken. N-Acetyl-β-anisidinopropionic acid (III) was prepared by acetylation of the ester I followed by hydrolysis of the ester group. The same acetyl derivative was also obtained by acetylation of the anisidinopropionic acid giving a neutralization equivalent of 410. Benzoylation of II with benzoyl chloride in sodium hydroxide solution resulted only in the isolation of benzanisidide. Benzoylation of I gave a product which, after hydrolysis of the ester group, gave an oil with a neutralization equivalent close to the theoretical.

Attempted benzylation of II resulted in the isolation of benzylanisidine or dibenzylanisidine in various experiments. Condensation of benzylanisidine with ethyl acrylate gave a good yield of ethyl N-benzyl-β-anisidinopropionate, although the latter was difficult to purify. Hydrolysis of the ester led to a dark oil for which no satisfactory method of purification could be found.

Reaction of II directly with tosyl chloride did not result in a crystalline product. However, reaction of I with tosyl chloride followed by hydrolysis of the ester gave tosyl-β-anisidinopropionic acid (IV) agreeing in melting point with that reported by Clemo and Perkin.[3] Condensation of tosyl anisidine with β-chloropropionic acid according to Clemo and Perkin[3] resulted in a poor yield of the acid, but by modification of the conditions the yield of acid was raised to 50%.

Ring closure experiments were carried out with the acetyl, benzoyl, benzyl and tosyl derivatives of β-anisidinopropionic acid using such reagents as sulfuric acid, phosphorus pentoxide, phosphorus oxychloride, etc. These were uniformly unsuccessful except as noted below. III with phosphorus pentoxide gave a small yield of material agreeing in melting point with that reported by Clemo and Perkin[3] for 4-hydroxy-6-methoxy-1,2-dihydroquinoline (V). With stannic chloride a very small yield of a substance not identical with III, although resembling it in melting point, was obtained. This material apparently was the result of further chlorination of the desired product. The benzyl derivative of II gave benzyl and dibenzyl anisidine as the only isolable products of ring closure experiments. Likewise only benzoyl anisidine resulted from similar experiments with the benzoyl derivative of II.

Ring closure experiments with IV furnished conflicting and unexplained results. The glassy tosyl derivative obtained directly from II, on treatment with phosphorus oxychloride, yielded a substance melting at 243–244° which gave analytical figures corresponding to those demanded for 1-tosyl-4-chloro-6-methoxy-1,2-dihydroquinoline (IV). However, a similar experiment with IV prepared by hydrolysis of the ethyl ester gave a substance of the same melting point but which depressed the melting point of the first substance and differed from it in solubility in benzene. Clemo and Perkin[3] report the formation of a mixture of VII and a compound presumably VI, in the light of Backeberg's reinterpretation,[4] when IV is treated with phosphorus oxychloride. They did not isolate either component from the mixture. The non-identity of the two supposedly 1-tosyl-4-chloro-6-methoxyquinolines obtained by us was further shown by the difference in melting points of the products obtained by hydrolysis of the tosyl group.

Our crystalline IV, which agreed in melting point with that of Clemo and Perkin,[3] likewise gave a substance agreeing in properties with the 1-tosyl-4-hydroxyquinoline reported by them when treated with phosphorus pentoxide. From this we conclude that our crystalline IV and substances derived from it probably parallel those of Clemo and Perkin. The nature of the high molecular weight II as well as of the glassy IV and substances derived from it encountered by us remains unexplained.

Finally, attempts were made to dehydrogenate the dihydroquinolines to quinolines using a variety of reagents such as bromine, palladiumized charcoal, arsenic pentoxide, lead peroxide, sulfur, etc. From the fact that these experiments were uniformly unsuccessful taken together with the expectation that a dihydroquinoline would either dehydrogenate readily or disproportionate to a quinoline and a tetrahydroquinoline, we believe that doubt is cast on the structures assigned to them. The investigation of these substances will be continued.

Experimental[5a,6]

Ethyl β-(*p*-Anisidino)-propionate, I.—To a mixture of 369 g. (3 moles) of commercial *p*-anisidine and 75 ml. of glacial acetic acid contained in a 3-liter three-necked flask equipped with stirrer, dropping funnel and reflux condenser was added 330 g. (3 moles) of redistilled ethyl acrylate with stirring on the steam-bath during the course of an hour. The mixture was stirred and heated on the bath for an additional eight to ten hours. The reaction mixture, deep red in color, was washed twice with an equal volume of water, then diluted with an equal volume of ether and washed with 500 ml. of 5% sodium bicarbonate solution. After washing again with water, drying and

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[5a] All melting and boiling points are corrected.

[6] Microanalyses by Misses Lois May and Frances Marx.

removing the solvent, the residual dark red oil was fractionated at reduced pressure. The fraction boiling at 153–158° (0.6 mm.) weighed 362 g. and consisted of the desired ester.

Anal. Calcd. for $C_{12}H_{17}NO_2$: N, 6.3. Found: N, 6.4.

The second fraction boiling at 175–185° (0.6 mm.) weighed 25 g. and is apparently N,N'-di-(β-carbethoxyethyl)-*p*-anisidine.

Anal. Calcd. for $C_{17}H_{25}NO_5$: C, 63.3; H, 7.8. Found: C, 63.0; H, 7.7.

Ethyl β-(*m*-Chloroanilino)-propionate.—This was prepared in the same manner as was I. The yield of the ester boiling at 155–160° (0.2 mm.) was 57%.

Anal. Calcd. for $C_{11}H_{14}ClNO_2$: C, 58.0; H, 6.2. Found: C, 58.1; H, 6.2.

The following comments on the preparation of both of the above esters may be made. Apparently the impure esters are not too stable; the addition reaction is reversible and dissociation into amine and ethyl acrylate occurs under certain conditions. Conversion into other products of undetermined nature also occurs. However, both esters can be prepared in yields of about 60% if care is taken in handling the products. Exposure to the air, distillation at pressures greater than 1 mm. and prolonged excessive heating during distillation appear to be the main causes of decomposition. If suitable precautions are observed, both esters are stable colorless liquids, which can be kept for weeks in amber bottles without change in boiling point.

Decomposition of **Ethyl β-(*p*-Anisidino)-propionate.**—Crude I from 4 moles of each reactant was distilled through an 8-in. packed column at a bath temperature of 255–257°. After a forerun of 63 g. boiling at 30° (0.6 mm.) had been taken off, the main fraction of 464 g. was collected at 193° (0.5 mm.). Continuous evolution of gas was noted during collection of the second fraction.

The residue in the distillation flask, amounting to about 125 ml. of dark brown liquid, solidified for the most part on standing overnight. Oil was sucked off from the solid on a sintered funnel and the solid was recrystallized from benzene forming pearly leaflets which melted at 135–136°. Although this melting point is close to that reported for *p*-acetanisidide, a mixture of the two showed a marked depression. The analytical data also did not agree with that for the latter substance.

Anal. Found: C, 68.3; H, 7.0.

The substance was not investigated further.

The second fraction was then exposed to water pump vacuum (15–20 mm.) at room temperature for several hours during which the weight decreased from 464 to 436 g. and solid separated. This was filtered off, washed with ether and melted at 80–85°. After recrystallization from carbon tetrachloride containing a little chloroform and finally from ethyl acetate, the substance formed small needles which melted at 86.5–88°. It was soluble in *N* hydrochloric acid, slightly soluble in ether, soluble in methyl and ethyl alcohols and insoluble in dilute ammonium hydroxide.

Anal. Found: C, 64.4; H, 7.2; N, 8.9.

It was not investigated further.

β-(*p*-Anisidino)-propionitrile.—Equimolecular quantities of *p*-anisidine and acrylonitrile were refluxed with acetic acid (25 ml. per mole) for twelve hours. The product was dissolved in ether, washed successively with water, 5% bicarbonate solution, dried and distilled. The yield of material boiling at 247° (0.7 mm.) was 70%. The substance appeared to be accompanied by a persistent contaminant which prevented attainment of completely satisfactory analytical figures.

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.2; H, 6.8; N, 15.9. Found: C, 67.7; H, 7.1; N, 14.9.

β-(*p*-Anisidino)-propionic Acid, II.—To a hot solution of 75 g. of sodium hydroxide in 200 ml. of water was added with stirring 100 g. of I. Stirring and refluxing were continued for thirty minutes after the mixture became homogeneous. After addition of 150 ml. of water, the cooled solution deposited a voluminous white precipitate of the sodium salt of the acid on scratching. The slurry was further diluted with 290 ml. of water and neutralized with external cooling to *p*H 4 with hydrochloric acid. Addition of ammonium sulfate (600 g.) in portions salted out the acid as a curdy tan solid which was air dried and exhaustively extracted with boiling benzene. Recrystallization of the material extracted by the benzene gave 47% of the acid melting at 87–88°.

Anal. Calcd. for $C_{10}H_{13}NO_3$: C, 61.5; H, 6.7; neut. equiv., 195. Found: C, 61.5; H, 7.0; neut. equiv., 198.

In one experiment similar to the above, except that boiling was continued for only thirty minutes, a 71% yield of acid was obtained. However, the melting point of this material could not be raised above 76–77°.

Anal. Found: C, 61.7; H, 6.7; neut. equiv., 194.

In another experiment in which 40% sodium hydroxide was used, an acid melting at 74–75° which gave the following analytical data was obtained.

Anal. Found: C, 62.9; H, 7.1; neut. equiv., 410.

Hydrolysis of β-(*p*-anisidino)-propionitrile with either acid or alkali gave only a small yield of the acid.

N-Tosyl-β-(*p*-anisidino)-propionic acid IV

(a) **From Ethyl β-(*p*-Anisidinopropionate).**—A mixture of 111.5 g. of I, 95 g. of tosyl chloride, 20 g. of sodium hydroxide and 500 ml. of water was warmed on the steam-bath with stirring until it became homogeneous (eight to ten hours). After two hours an additional 20 g. of sodium hydroxide in 100 ml. of water was added. The precipitate which formed on acidification was warmed with dilute sodium carbonate solution and filtered from tosyl anisidine (42 g.) (possibly arising from decomposition of the acid or ester). On acidification of the filtrate, the product (60 g.) separated, and melted at 81–82° after recrystallization from benzene. This agrees with the melting point reported by Clemo and Perkin[3] for the same acid.

(b) **By Condensation of Tosyl Anisidine and Ethyl β-Chloropropionate.**—This is the method of Clemo and Perkin[3]; however, following their procedure we obtained only a 15% yield. Modification of their procedure by (a) using sufficient sodium hydroxide to keep the tosylanisidine in solution, (b) lowering the reaction temperature to 90° and (c) extending the time of the reaction to twenty-four hours, gave a 50% yield of material melting at 81–82° after recrystallization from benzene.

Attempts at the reaction of β-(*p*-anisidino)-propionic acid directly with tosyl chloride gave only non-crystalline glasses.

Ethyl N-Benzyl-β-(*p*-anisidino)-propionate.—A mixture of 42.6 g. of benzylanisidine, 20 g. of ethyl acrylate and 5 ml. of glacial acetic acid was refluxed for twelve hours, washed successively with water and sodium bicarbonate solution and then distilled, yielding 90% of material boiling at 179–180° (0.4 mm.).

Anal. Calcd. for $C_{19}H_{23}NO_3$: C, 72.9; H, 7.4. Found: C, 73.5; H, 7.4.

Hydrolysis of the ester gave the acid as a dark oil which could not be distilled.

N-Acetyl-β-(*p*-anisidino)-propionic Acid, III.—A mixture of 27 g. of II (m. p. 72°, neut. equiv., 410), 100 ml. of acetic acid and 19 ml. of acetic anhydride was refluxed for three hours. The solvents were removed at the water pump and the residue crystallized on cooling and seeding. A small amount of residual oil was removed from the crystalline material (22 g.) by washing with ether. Recrystallization from ethyl acetate gave the acetyl acid melting at 86.5–88.5°.

Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.7; H, 6.4; neut. equiv., 240. Found: C, 60.4; H, 6.6; neut. equiv., 237.

The same acetyl derivative was also prepared by refluxing 28.8 g. of I, 90 ml. of acetic acid, 19 ml. of acetic anhydride and 4 ml. of sulfuric acid (sp. gr. 1.84) for six hours. Most of the acetic acid was removed at the water pump and the chloroform solution of the residue was washed with water. The residue, after removal of the chloroform, was warmed for ten minutes on the steam-bath with 50 g. of 17% sodium hydroxide solution. On acidification with hydrochloric acid, the acetyl derivative separated as an oil which was extracted with chloroform and recrystallized from ethyl acetate. The yield of material identical with that prepared from the high molecular weight acid as above and melting at 86–88° was 19.3 g. (63%); neutral equiv. found, 240.

N-Benzoyl-β-(*p*-anisidino)-propionic Acid.—Benzoylation of I with benzoyl chloride in 65% alcohol in the presence of sodium acetate at 10° followed by hydrolysis of the ester with 15% sodium hydroxide solution gave the N-benzoyl derivative of anisidinopropionic acid as a dark red oil in 76% yield. No satisfactory method of purification was found. Neutral equiv. of the crude oil: calcd., 299. Found: 305.

Reaction of N-Acetyl-β-(*p*-anisidino)-propionic Acid with Phosphorus Pentoxide.—A mixture of 25.3 g. of III, 25 g. of diatomaceous earth (Hyflo-Supercel), 75 g. of phosphorus pentoxide and 350 ml. of dry xylene was refluxed for three hours. The neutral fraction (6.5 g.) could not be crystallized and was boiled for two hours with 17 ml. of acetic acid and 20 ml. of hydrochloric acid (sp. gr. 1.19) for hydrolysis of the acetyl group. Distillation of the product gave a solid distillate melting at 113–114°. Clemo and Perkin,[3] report 4-hydroxy-6-methoxy-1,2-dihydroquinoline melting at 112°. If the Supercel is omitted, none of the crystalline material is obtained.

Reaction of N-Acetyl-β-(*p*-anisidino)-propionic Acid with Stannic Chloride.—A mixture of 29.2 g. of III and 28.2 g. of phosphorus pentachloride in 125 ml. of dry benzene, originally at 0° was allowed to stand at room temperature for two hours and then warmed on the steam-bath for five minutes. To the mixture at 0° was added a cold solution of 100 g. of stannic chloride in 100 ml. of dry benzene. After standing forty-five minutes at 0°, hydrolysis gave an oily neutral fraction (0.5 g.) which crystallized from methanol. On recrystallization from the same solvent, it melted at 115.5–116.5°. A mixture of this substance with that obtained above melted at 90–110°. Analysis indicated that chlorination had occurred. The figures agreed with those for a 1-acetyltrichloro-6-methoxydihydroquinoline.

Anal. Calcd. for $C_{12}H_{10}Cl_3NO_2$: C, 47.0; H, 3.3; N, 4.6. Found: C, 47.5; H, 3.4; N, 4.4.

Action of Phosphorus Oxychloride on N-Tosyl-β-(*p*-anisidino)-propionic Acid.—A mixture of the glassy tosyl derivative (10 g.) prepared directly from the acid, and phosphorus oxychloride was warmed on the steam bath for fifteen minutes. After removal of the excess reagent by distillation, the residue was extracted with sodium carbonate solution, and the insoluble material was crystallized from alcohol and then from alcohol-benzene yielding 2 g. of material melting at 243–244° (Compound A) which furnished analytical figures agreeing with those required by 1-tosyl-4-chloro-6-methoxy-1,2-dihydroquinoline.

Anal. Calcd. for $C_{17}H_{16}ClNO_3S$: C, 58.5; H, 4.3; Cl, 10.2. Found: C, 58.5; H, 4.2; Cl, 9.9.

When the above experiment was repeated with IV, prepared from the ester and melting at 81–82°, a corresponding amount of a substance melting at 242–243° (Compound B) was obtained. However, a mixture of A and B melted at 220–230° and, whereas A was readily soluble in benzene, B was practically insoluble.

The tosylanisidinopropionic acid from which B was prepared yielded a compound melting at 124–125° when treated with phosphorus pentoxide in toluene[3] which agrees in m. p. with the 1-tosyl-4-hydroxy-6-methoxy-1,2-dihydroquinoline reported by Clemo and Perkin.[3]

Hydrolysis of the above compound with hydrochloric–acetic acid gave 4-hydroxy-6-methoxy-1,2-dihydroquinoline melting at 112–113° in agreement with Clemo and Perkin.[3]

Hydrolysis of A and B.—A mixture of 5 g. of A, 20 ml. of acetic acid and 30 ml. of hydrochloric acid (sp. gr. 1.19) was refluxed for four hours. The residue after removal of the solvent was purified by dilution of its solution in acetic–hydrochloric acid (1:1). It melted over 300°. On treatment of the material with aqueous alkali, it passed into an oil from which it was recovered on acidification. It was insoluble in the usual organic solvents.

Anal. Calcd. for $C_{10}H_{10}ClNO$: C, 61.4; H, 5.1. Found: C, 61.7; H, 4.9.

Similar treatment of B gave a substance which was soluble in alcohol and melted at 239° after recrystallization from acetic acid.

Anal. Calcd. for $C_{10}H_{10}ClNO$: C, 61.4; H, 5.1. Found: C, 62.0; H, 4.9.

Summary

1. The preparation of β-(*p*-anisidino)-propionic acid by addition of *p*-anisidine to ethyl acrylate and to acrylonitrile followed by hydrolysis has been investigated.

2. Ring closure of derivatives of β-(*p*-anisidino)-propionic acid to quinoline derivatives has also led to results difficult to interpret.

3. Ethyl β-(*m*-chloroanilino)-propionate has been prepared.

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