acetic acid, complete reaction occurred in 25 min. Unlike the 11-ketone case, a substantial amount of 3-acetylation occurred during the reaction. The debromination was carried out as previously described.[7] The mixed 3-alcohol and 3-acetate, 22.2 g. in 1.11 l., of methanol was treated with 22.2 g. of potassium bicarbonate in 222 ml. of water and refluxed in a nitrogen atmosphere for 1 hr. The cooled mixture was diluted with 7 l. of ice-water and after standing overnight was filtered. The 18.9 g. of crystalline product was collected and recrystallized from acetone to give 17.1 g. of diol, m.p. 203–205°, $[\alpha]_D^{25}$ −19.3°.

Anal. Calcd. for $C_{21}H_{30}O_4$: C, 72.81; H, 8.73. Found: C, 72.83; H, 8.85.

21-Acetoxy-17α-hydroxy-5-pregnene-3,12,20-trione, III. The trioldione monoacetate, IV, 135 mg. dissolved in 25 ml. of acetone (redistilled from potassium permanganate), was cooled to 10° and stirred with 0.10 ml. of an aqueous solution containing 26.7 mg. of chromium trioxide and 0.023 ml. of sulfuric acid.[23] Within 1 min. a gray-green precipitate formed. Stirring was continued an additional 2 min. and the reaction mixture was diluted to 150 ml. with nearly saturated sodium chloride solution. The crystalline precipitate filtered off weighed 130 mg., melted at 155°, and showed no selective ultraviolet absorption maximum and no band at 6 μ in the infrared. The analytical sample was recrystallized from water containing 20% of acetone and finally from hexane, m.p. 172–175°, $[\alpha]_D^{25}$ +8.2°.

Anal. Calcd. for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 68.30; H, 7.71.

Isomerization of 21-acetoxy-17α-hydroxy-5-pregnene-3,12,20-trione (III) *to the corresponding 4-ene* (II). The 5-ene, III, 600 mg. was stirred and refluxed 2 hr. in 30 ml. of dry acetone with 1.2 g. of potassium acetate. The mixture was cooled, diluted with 60 ml. of water, and concentrated under reduced pressure to 60 ml. final volume. The crystalline precipitate was collected and recrystallized from hexane containing a small proportion of acetone. The product, II, needles melted from 191–193°, $[\alpha]_D^{25}$ +123°, $\lambda_{max}^{CH_2OH}$ 238 mμ, log ε = 4.23, agreed well with the product described above and with the preparation reported by the British group.[10]

21-Acetoxy-5α,6β-dibromo-3β,17α-dihydroxy allopregnane-12,20-dione (V). A solution of 1 g. of 21-acetoxy-3β,17α-dihydroxy-5-pregnene-12,20-dione, α_D −13.7°, in 25 ml. of methylene chloride at 4° was treated with 10.72 ml. of a carbon tetrachloride solution containing a molar equivalent of bromine. The bromine solution was added at a controlled rate during 75 min. time. The mixture was stirred an additional 2 min., solvents were removed *in vacuo* at room temperature and 10 ml. of methanol was added. On stirring, 955 mg. of colorless crystals of V, α_D −28.8°, m.p. 140–141° dec., deposited. A small additional crop separated from the decanted supernatant solution. Some preparations of the dibromide developed coloration on standing due to decomposition. Purer preparations were more stable.

Anal. Calcd. for $C_{23}H_{32}O_6Br_2$: C, 48.95; H, 5.72; Br, 28.32. Found: C, 49.12; H, 5.86; Br, 28.77.

Treatment of the dibromide, V, *with perbenzoic acid.* The dibromide, V, 1.17 g., dissolved in 7.9 ml. of cold chloroform, was treated with 11 ml. of a solution of perbenzoic acid in the same solvent (1 ml. = 11.52 ml. 0.1*N* sodium thiosulfate) 0.2 ml. of water, and 0.45 ml. of 10% sulfuric acid in acetic acid and was let stand with occasional shaking for 113 hr. in the dark at room temperature. The resulting orange solution was shaken with 100 ml. of ether and 100 ml. of water. Decolorization occurred and the aqueous phase was discarded. The organic layer was washed with aqueous sodium iodide to destroy peroxyacid and was washed cautiously with just enough dilute sodium thiosulfate to decolorize the large excess of liberated iodine, with dilute sodium bicarbonate to remove acids and with saturated sodium chloride solution. Solvents were evaporated under reduced pressure. The residue, dissolved in 25 ml. of acetone, was stirred with 2 g. of potassium iodide and refluxed for 1 hr. After dilution with water, extraction with ether, and removal of liberated iodine by treatment with dilute sodium thiosulfate, the isolated steroid was chromatographed on Florisil.[14] Elution with methylene chloride gave unchanged starting material identified by its infrared spectrum. Further elution with 1:1 methylene chloride gave an intermediate cut rich in unreacted starting material. Elution with 4% methanol in methylene chloride gave 250 mg. of a material yielding an amorphous powder on treatment with ether and having a single broad carbonyl infrared absorption band from 5.7 to 5.8 μ with a weak shoulder at 5.91 μ (in methylene chloride solution). The carbonyl area resembled that of the similarly obtained known 5α—C ring lactonoid corticoid.[13] The substance gave a strong tetrazolium color reaction.

PHILADELPHIA 18, PA.

(23) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN CO.]

Microbiological Transformations of Steroids. XVI. Multiple Oxidation of the Steroid Nucleus[1]

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Received March 23, 1960

Two cases of microbial hydroxylation with accompanying oxidation of a pre-existing 11β-hydroxyl group are reported. *Cunninghamella blakesleeana* [A.T.C.C. 8688a (+)] and *Helicostylum piriforme* (A.T.C.C. 8992) were found to convert 11β,21-dihydroxypregna-4,17(20)-dien-3-one (I) to 9α,21-dihydroxypregna-4,17(20)-diene-3,11-dione (II). *Rhizopus arrhizus* (A.T.C.C. 11145) was found to convert the same substrate to 6β,21-dihydroxypregna-4,17(20)-diene-3,11-dione (V). Proof of structures of the two products consisted in their conversion to the known 9α-hydroxy- and 6β-hydroxycortisone acetates, respectively.

DISCUSSION

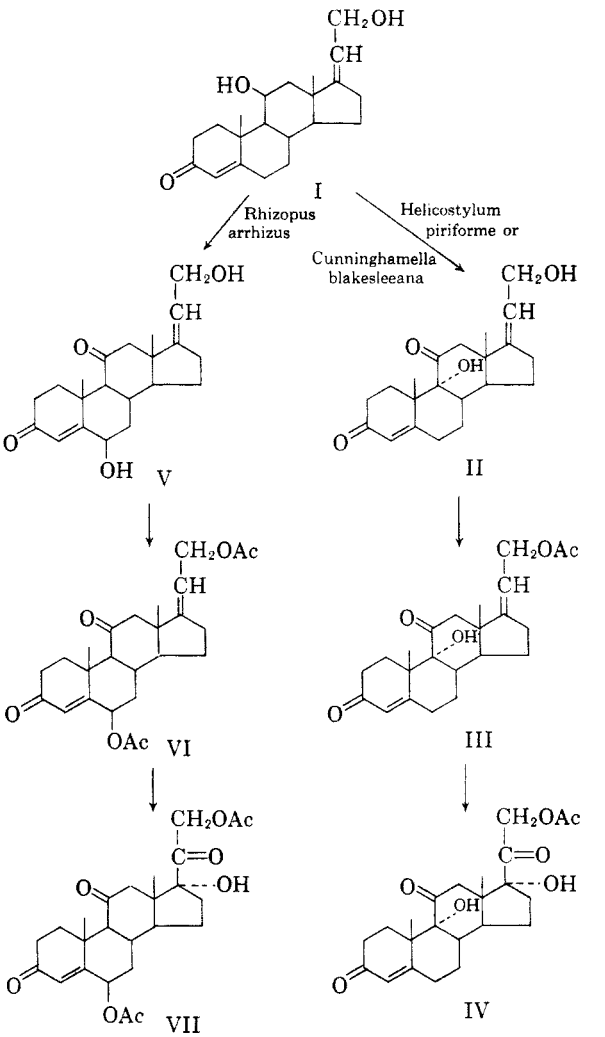
In our continuing investigation of the microbial transformation of steroids, we became interested in determining the positions susceptible to attack by various microorganisms in a steroid containing both a conjugated and an isolated

(1) Paper XV of this series, *J. Am. Chem. Soc.*, **80**, 3382 (1958).

double bond. The substrate used for these studies was 11β,21-dihydroxypregna-4,17(20)-diene-3-one (I)[2] (hereafter called dienediol), chosen because the 11 position is blocked, thus decreasing the number of possible products.

Both *Cunninghamella blakesleeana* [A.T.C.C. 8688a (+)] and *Helicostylum piriforme* Bain (A.T.C.C. 8992) have been shown to perform 14-hydroxylation.[1] When the dienediol (I) was incubated with either of these organisms one major product was formed. Although other products were also formed to some degree in both fermentations, the *Helicostylum* gave a much cleaner transformation than did the *Cunninghamella*. The major product, purified by chromatography and recrystallization, differed from the substrate by the presence of an added carbonyl group, shown by the infrared spectrum and elemental analysis. Acetylation produced a monoacetate (III) whose infrared spectrum showed the presence of a free hydroxyl, an ester, and a 1:1 ratio of α,β-saturated ketone to α,β-unsaturated ketone. On the basis of the above data it was hypothesized that oxidation of the 11β-hydroxyl group as well as hydroxylation at C-14 had occurred during the fermentation. The final proof of structure consisted in treatment of the acetate (III) in *t*-butyl alcohol–pyridine with phenyl iodosoacetate in the presence of catalytic amounts of osmium tetroxide[3] to convert the 17-(20)-double bond to a 17α-hydroxy-20-ketone. The supposition that the compound was hydroxylated cortisone acetate was borne out by elemental analysis, infrared and ultraviolet spectra, positive Tollens' test, and papergram mobilities. However, the properties of the compound did not agree with those of the expected 14α-hydroxy cortisone acetate[3] but were identical with those of 9α-hydroxy cortisone acetate (IV) prepared by the oxidation of 9α-hydroxyhydrocortisone acetate,[4] obtained *via* the 9,11-oxide.

The introduction of a hydroxyl group into a steroid molecule with accompanying oxidation of a pre-existing hydroxyl had previously been noted in the case of testosterone. Incubation of this steroid with *Fusarium sp.*[5] resulted in the introduction of a hydroxyl into the 15α-position with concurrent oxidation of the 17β-hydroxyl to a ketone to give 15α-hydroxyandrost-4-ene-3,17-dione. No case, however, has been reported on the oxidation of a 11β-hydroxy steroid to an 11-ketosteroid by a microorganism. The microbial oxidation[6] of Reichstein's Compound S (11-desoxy-



17α-hydroxycorticosterone) with *Cunninghamella blakesleeana* is known to produce both hydrocortisone and cortisone; however, no evidence has been presented to show whether cortisone is a primary or secondary product of the fermentation. We have now shown in shake flask studies the conversion of hydrocortisone to cortisone with this organism, thus establishing the possible route to cortisone in the above fermentation as one involving oxidation of the newly formed 11β-hydroxyl group. The introduction of a hydroxy group into the 9 (or 8) position of a steroid by a microorganism has been reported by several groups.[7] The present

(2) J. A. Hogg, P. F. Beal, A. H. Nathan, F. H. Lincoln, W. P. Schneider, B. J. Magerlein, A. R. Hanze, and R. W. Jackson, *J. Am. Chem. Soc.*, **77**, 4436 (1956).

(3) E. J. Agnello, B. L. Bloom, and G. D. Laubach, *J. Am. Chem. Soc.*, **77**, 4684 (1955).

(4) J. Fried and E. F. Sabo, *J. Am. Chem. Soc.*, **79**, 1130 (1957).

(5) P. D. Meister, H. C. Murray, R. C. Meeks, A. Weintraub, S. H. Eppstein, L. M. Reineke, H. M. Leigh Osborn, and D. H. Peterson, unpublished data.

(6) F. R. Hanson, L. M. Mann, E. D. Nielson, H. V. Anderson, M. P. Brunner, J. R. Karnemaat, D. R. Colingsworth, and W. J. Haines, *J. Am. Chem. Soc.*, **75**, 5369 (1953).

(7a) D. Stone, M. Hayano, R. I. Dorfman, O. Hechter, C. R. Robinson, and C. Djerassi, *J. Am. Chem. Soc.*, **77**, 3926 (1955); (b) J. Fried, R. W. Thoma, D. Perlman, J. E. Herz, and A. Bowman, *Recent Progr. in Hormone Research*, **11**, 157 (1955), Academic Press, Inc., New York, N. Y.; (c) A. Schubert, D. Onken, R. Siebert, and K. Heller, *Helv. Chim. Acta*, **91**, 2549 (1958); (d) G. Rosenkranz, O. Mancera, and F. Sondheimer, *J. Am. Chem. Soc.*, **76**, 2227 (1957);(e.)R. M. Dodson and R. D. Muir, *J. Am. Chem. Soc.*, **80**, 6148 (1958).

example, however, represents, to our knowledge, the first example of the introduction of a hydroxyl group into a steroid molecule with accompanying oxidation of a pre-existing 11β-hydroxyl to an 11-ketone.

Microbial oxidation of the dienediol (I) with *Rhizopus arrhizus* Fischer (A.T.C.C. 11145) also yielded a compound in which a hydroxyl was introduced with concurrent oxidation of the pre-existing hydroxyl group. The product was identified as 6β,21-dihydroxypregna-4,17(20)-diene-3,11-dione (V) on the basis of the following evidence. The compound exhibited infrared absorption bands at 3500 cm.$^{-1}$, 3410 cm.$^{-1}$, 1697 cm.$^{-1}$, 1667 cm.$^{-1}$, and 1617 cm.$^{-1}$. An examination of the spectrum indicated that the compound contained hydroxyl and a 1:1 ratio of α,β-saturated to α,β-unsaturated ketone. The ultraviolet spectrum showed a maximum at 233 mμ with ε 13,850, which is in agreement with that reported for other 6β-hydroxylated steroids.[8] The compound on acetylation formed a diacetate (VI) as evidenced by analysis and infrared spectrum. Final proof consisted in the conversion of the diacetate (VI) to the known 6β-hydroxycortisone diacetate[9] by reaction with phenyl iodosoacetate in the presence of osmium tetroxide.[2]

Hydroxylation of steroids at carbon atom 6 is one of the most common reactions of the fungi and has been reported to occur with numerous genera of the order of Mucorales. The microorganism of the present study, *Rhizopus arrhizus*, converts[10] progesterone to 6β,11α-dihydroxyprogesteron. The conversion of the dienediol (I) to 6β,21-dihydroxypregna-4,17(20)-diene-3,11-dione (V) could thus be represented as a 6β,11α-dihydroxylation to give the 6β-hydroxy-11-ketone.

EXPERIMENTAL[11]

9α,21-Dihydroxypregna-4,17(20)-diene-3,11-dione (II). A fermenter containing 100 l. of a sterile medium at *p*H 4.9, made from commercial dextrose (10 g./l.) and corn steep (20 g./l.), was inoculated with 5.0 l. of vegetative growth of *Helicostylum piriforme* Bain (A.T.C.C. 8992). After 24 hr. of vigorous agitation and aeration at a rate of 20 l. per min. at 28°, 20.0 g. of 11β,21-dihydroxypregna-4,17(20)-diene-3-one (I) was added in 500 ml. of acetone, and the fermentation continued for 48 hr. under the same conditions. Extraction of the conversion products with methylene chloride and work-up as described previously[10] yielded *ca.* 42.0 g. of a semicrystalline residue. Paper chromatography, using the PTF system[12] indicated the presence of a new compound with increased polarity.

The semicrystalline residue was redissolved in *ca.* 1000 ml. of dry methylene chloride and chromatographed on 2000 g. of Florisil,[13] taking six 2-l. fractions of the following solvent mixtures: 18%, 20%, 25%, and 50% acetone in petroleum ether (b.p. 62–72°). Fractions 9–21 were combined, dissolved in hot acetone, treated with Darco G-60 (2 g.), filtered, and the filtrate concentrated until copious crystallization took place. The mixture was cooled in a refrigerator for 2–3 hr., and filtered to give 10.33 g. of II melting at 217–219°. Additional crops of 1.62 g. (m.p. 216–218°) and 360 mg. (m.p. 211.5–214°) were obtained upon further concentration of the initial filtrate, making the over-all yield 12.31 g. (59.0%). Recrystallization from acetone gave material melting at 219.5–221°, $[\alpha]_D$ +173° (*c* 1.022, dioxane); $\lambda_{max}^{alc.}$ 238.5 mμ (15,725); λ_{max}^{Nujol} 3440, 3220, 1697, 1635, and 1603 cm.$^{-1}$

Anal. Calcd. for $C_{21}H_{28}O_4$ (344.43): C, 73.22; H, 8.19. Found: C, 73.32; H, 8.30.

9α,21-Dihydroxypregna-4,17(20)-diene-3,11-dione 21-acetate (III). To a solution of 5.0 g. of 9α,21-dihydroxypregna-4,17(20)-diene-3,11-dione (II) in 15 ml. of dry pyridine at 20° was added 15 ml. of acetic anhydride. After 17 hr. at room temperature the solution was poured into 450 ml. of ice-water mixture. The crystalline product which separated was filtered, washed well with water, and dried; yield 5.53 g. (99.0%), m.p. 172.5–177°. The crystals were dissolved in 70 ml. of hot acetone, the solution clarified and concentrated on a steam bath until crystallization began. The mixture was cooled in a refrigerator and filtered to give 3.83 g. of III, m.p. 188.5–190°, $[\alpha]_D$ +160° (*c* 0.65, acetone), $\lambda_{max}^{alc.}$ 239 mμ (15,750); λ_{max}^{Nujol} 3390, 1725, 1700, 1652, 1623, 1240, and 1224 cm.$^{-1}$

Anal. Calcd. for $C_{23}H_{30}O_5$ (386.47): C, 71.48; H, 7.82. Found: C, 71.42; H, 8.19.

9α-Hydroxycortisone acetate (IV). To an ice-cold solution of 387 mg. (1 mmole) of 9α,21-dihydroxypregna-4,17(20)-diene-3,11-dione 21-acetate (III) in 18.5 ml. of *t*-butyl alcohol containing 0.93 ml. of pyridine and 0.185 ml. of water was added 370 mg. of *N*-methylmorpholine oxide, 800 mg. of phenyl iodosoacetate, and 4.0 mg. of osmium tetroxide. The slurry was stirred at 0–5° for 2 days at which time the reaction mixture was clear. Magnesol[14] (600 mg.) and a solution of 150 mg. of sodium sulfite in 10 ml. of water were added, and the mixture stirred for 15 min. at room temperature. The mixture was filtered and the filtrate concentrated to opalescence under reduced pressure. The solution was cleared by careful addition of *t*-butyl alcohol and stirred at room temperature for 1 hr. The crystals which formed were filtered and washed with *t*-butyl alcohol–water (1:4) and finally water, and dried; yield 245 mg. (58.5%), m.p. 233–236°.[15] Recrystallization from acetone–petroleum ether (b.p. 62–72°) gave 185 mg., m.p. 237–239°, $[\alpha]_D$ +227° (*c* 0.48, $CHCl_3$), $\lambda_{max}^{alc.}$ 239 mμ (15,900), reported[4] m.p. 237–239°, $[\alpha]_D^{23}$ +211° (*c* 0.51, $CHCl_3$), $\lambda_{max}^{alc.}$ 238 mμ (16,500). The compound has an infrared spectrum identical with that of a sample of 9α-hydroxycortisone acetate prepared by the oxidation of 9α-hydroxyhydrocortisone acetate, obtained *via* the 9,11-oxide,[4] with sodium dichromate in acetic acid by W. P. Schneider of these laboratories with λ_{max}^{Nujol} 3400, 1748, 1732, 1710, 1660, 1620, and 1239 cm.$^{-1}$

6β,21-Dihydroxypregna-4,17(20)-diene-3,11-dione (V). 11β,21-Dihydroxypregna-4,17(20)-diene-3-one (I—2.5 g.) was fermented with *Rhizopus arrhizus* (A.T.C.C. 11145)

(8) P. T. Herzig and M. Ehrenstein, *J. Org. Chem.*, **16**, 1050 (1951).

(9) S. Burstein and R. I. Dorfman, *J. Biol. Chem.*, **213**, 581 (1955).

(10) D. H. Peterson, H. C. Murray, S. H. Eppstein, L. M. Reineke, A. Weintraub, P. D. Meister, and H. M. Leigh, *J. Am. Chem. Soc.*, **74**, 5933 (1952).

(11) All melting points were taken in open capillaries and are not corrected for stem exposure. The fermentation procedures using *Cunninghamella blakesleeana* and *Rhizopus arrhizus* were identical to that given for *Helicostylum piriforme*.

(12) A. Zaffaroni, R. B. Burton, and E. H. Keutman, *J. Biol. Chem.*, **193**, 749 (1951).

(13) A synthetic magnesium silicate manufactured by the Floridin Co., Warren, Pa.

(14) Magnesium silicate formerly manufactured by Westvaco-Chlor-Alkali Division, Food, Machinery and Chemical Corp., New York.

(15) A polymorphic modification melted at 212–214°.

in the same manner as that given for the *Helicostylum* fermentation above. The semicrystalline residue obtained upon evaporation of the extraction solvent showed by papergram[12] one major product which was more polar than I and differed in mobility from that produced by the *Helicostylum*. The residue was triturated with acetone and filtered to give 610 mg. of crystals. These were dissolved in 65 ml. of hot acetone, filtered through a bed of Magnesol,[14] and concentrated to crystallization; yield of V, 360 mg., m.p. 252–254°, $[\alpha]_D^{23}$ −107° (*c* 0.86, dioxane), $\lambda_{max}^{alc.}$ 233 mμ (13,850), λ_{max}^{Nujol} 3500, 3410, 1697, 1667, and 1617 cm.$^{-1}$

Anal. Calcd. for $C_{21}H_{28}O_4$ (344.43): C, 73.22; H, 8.19. Found: C, 73.53; H, 8.47.

The mother liquors were combined, concentrated to remove the acetone, and chromatographed on 300 g. of Florisil,[13] taking five 200-ml. fractions of each of the following solvents: methylene chloride, 12%, 20%, 30%, and 50% acetone in petroleum ether (b.p. 62–72°). Fractions 17–21 (1.21 g.) were combined and crystallized from acetone to give 500 mg. of V, melting at 243–247°. Recrystallization of this material from acetone gave 400 mg. with m.p. 246–250°.

6β,21-Dihydroxypregna-4,17(20)-diene-3,11-dione diacetate (VI). A solution of 400 mg. of V in 1 ml. of pyridine and 1 ml. of acetic anhydride was allowed to react overnight at room temperature. Addition of ice and water caused crystallization. The mixture was filtered and the solid dried, yield 440 mg., m.p. 129–135°. Recrystallization from ethyl acetate (1 ml.) and petroleum ether (b.p. 62–72°) (2 ml.) gave 270 mg., m.p. 136–138.5°, $[\alpha]_D$ +66° (*c* 0.72, dioxane), $\lambda_{max}^{alc.}$ 231 mμ (13,250), λ_{max}^{Nujol} 1732, 1700, 1676, 1617, 1250, and 1230 cm.$^{-1}$

Anal. Calcd. for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 69.70; H, 7.90.

6β-Hydroxycortisone 6,21-diacetate (VII). 6β,21-Dihydroxypregna-4,17(20)-diene-3,11-dione diacetate (580 mg.) was oxidized with phenyliodosoacetate in the presence of osmium tetroxide to yield 400 mg. of 6β-hydroxycortisone 6,21-diacetate by a procedure identical with that given above for the preparation of 9α-hydroxycortisone acetate. Recrystallization from acetone–petroleum ether (b.p. 62–72°) gave 260 mg., m.p. 236–238.5° (reported[12] 225–233°), $[\alpha]_D^{23}$ +124° (*c* 0.33, dioxane), λ_{max}^{Nujol} 3540, 1735, 1712, 1697, 1675, 1620, and 1240 cm.$^{-1}$ The ultraviolet spectrum in sulfuric acid agrees with that given by Burstein and Dorfman.[9] A sample obtained by chromic acid oxidation of 6β-hydroxyhydrocortisone 6,21-diacetate, prepared *via* the 5,6-oxide by G. B. Spero of these laboratories, melted at 231–232°, $[\alpha]_D^{23}$ +127° (dioxane) and was identical with our sample by infrared and paper chromatographic analysis.

Acknowledgment. The authors are indebted to A. Koning for technical assistance; to L. M. Reineke and group for papergram analysis; to Dr. J. L. Johnson, J. E. Stafford, and Mrs. G. S. Fonken for infrared and ultraviolet absorption studies; and to W. A. Struck and associates for analytical data.

KALAMAZOO, MICH.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF HOWARD UNIVERSITY]

Ultraviolet Spectroscopic Studies of Some Sweet and Nonsweet Isomeric *m*-Nitroanilines[1]

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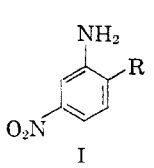
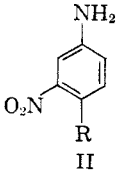
The ultraviolet spectra of some 2- and 4-substituted 5-nitroanilines and of their respective disubstituted constituent compounds have been measured in 95% alcohol. Their absorption bands have been classified and discussed in terms of electronic transitions within the molecules. Certain solvent and salt effects are also reported. Taste-structure relationships which possibly might be drawn from the spectra are pointed out.

It has been observed[3] that many 2-substituted 5-nitroanilines (I) are intensely sweet, whereas the isomeric 4-substituted-5-nitroanilines (II) are bitter or tasteless.



I



II

Relative sweetness[4]
(Sucrose = 1)

R	I	II
$-OCH_3$	167	Tasteless
$-CH_3$	298	Tasteless
$-Br$	715	Tasteless

This striking difference in taste of isomeric pairs has aroused our interest in their physicochemical properties and the present paper reports some of their spectroscopic properties. There is even a noticeable difference in the color of the isomers. All of the compounds are yellow to red but the sweet isomer of each couple is lighter than the nonsweet member.

Two types of spectroscopic studies were made in this investigation. The first was to measure the complete ultraviolet spectra down to 210 mμ. It was hoped, through an interpretation of the spectra, to learn if there is any significant difference in electronic interactions of the substituents in the

(1) Number V in a program of physicochemical studies of the sense of taste; No. IV, *J. Org. Chem.*, **25**, 1220 (1960).

(2) Taken from the M.S. thesis of L.G.C., Howard University, 1959.

(3) J. J. Blanksma and P. W. M. van der Weyden, *Rec. trav. chim.*, **59**, 629 (1940); **65**, 329 (1946); *cf.* P. E. Verkade, *et al.*, *Rec. trav. chim.*, **68**, 639 (1949) and earlier papers in this series.