acid and persist throughout the series of mixtures. The three bands marked L diminish as the linoleic acid concentration decreases and the strong band O increases with the concentration of oleic acid.

The technique of low temperature infrared spectrometry does not lend itself easily to accurate measurements of band intensity, but mixtures of oleic and linoleic acids might be analyzed by matching the solid phase spectra with an atlas of the spectra of standard mixtures. For this purpose it would probably be sufficient to solidify the samples with solid carbon dioxide, as it is observed that on warming a sample cooled with liquid nitrogen the sharp characteristic structure persists until the compound approaches the melting point. Attention has been drawn previously to the effects of polymorphism on fatty acid spectra[7] and precautions must be taken in the preparation of samples to avoid complications due to polymorphism or compound formation and to recognize such if they should occur.[22]

(22) In Fig. 9 the mixture containing 0 2 mole fraction of linoleic acid possesses a band (M) not present in either of the constituent acids which may indicate complex formation although this would not be anticipated on the basis of melting point data. See K. S. Markley, "Fatty Acids," Interscience Publishers, Inc., New York, N. Y., 1947, p. 126.

The spectra of the solid brominated acids derived from oleic, linoleic and linolenic acids also exhibit large differences, especially between 450 and 700 cm.$^{-1}$ which could provide a basis for the analysis of mixed unsaturated acids, but while such a procedure would avoid the necessity of working at low temperature it would introduce the same uncertainties concerning the yields of brominated acids as complicate the interpretation of polybromide numbers.

Acknowledgments.—The authors wish to thank Dr. J. B. Brown of the Ohio State University for supplying samples of linoleic acid, linolenic acid and methyl arachidonate, and Mr D. S Keir and Mr. R. Lauzon for technical assistance in the determination of the spectra. The investigation was supported by a grant from The Ontario Cancer Treatment and Research Foundation, which is gratefully acknowledged.

OTTAWA, CANADA RECEIVED NOVEMBER 1 1951

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

Cortisone Intermediates. I. A New Preparation of 12α-Bromo-24,24-diphenylchol-23-en-3α-ol-11-one Acetate

BY E. B. HERSHBERG, HERSHEL L. HERZOG, STEPHEN B. COAN, LOIS WEBER AND MARGARET JEVNIK

A method derived from Gallagher's synthesis of dimethyl 12α-bromo-3α-succinoxy-11-ketocholanate from desoxycholic acid is applied to the synthesis of 12α-bromo-24,24-diphenylchol-23-en-3α-ol-11-one acetate, an intermediate in the Kendall synthesis of cortisone. The preparation and some reactions of the 12-phosphite and 12-sulfite esters of 24,24-diphenylchol-23-en-3α,12β-diol-11-one 3-acetate are described.

In common with all of the partial syntheses of cortisone from desoxycholic acid (I), that devised by Kendall and co-workers suffers from the multiplicity of steps required to shift the oxygen function from C-12 to C-11.[1] After eleven steps, by way of a Δ^{11}-system,[2] the hydroxyl group at C-12 is transformed into the ketone group at C-11, in 12α-bromo-24,24-diphenylchol-23-en-3α-ol-11-one acetate (IX). The same approach was used by Reichstein and co-workers,[3] in their synthesis of dehydrocorticosterone.

Gallagher and co-workers[4] developed a simpler process for transferring the oxygen from C-12 to C-11 which, starting with desoxycholic acid, led to dimethyl 12α-bromo-3α-succinoxy-11-ketocholanate (III) in seven steps. While methods have been suggested for incorporating this product into several schemes for the synthesis of cortisone, its use has not been reported. It is significant that the reaction of methyl 12α-bromo-3α,9α-epoxy-11-ketocholanate[1b,5] with excess phenylmagnesium bromide results in the reductive removal of bromine at C-12. From this it may be inferred that an attempt to prepare IX from III by reaction with phenylmagnesium bromide, followed by acetylation, also would result in the reductive loss of the C-12 bromine. In our laboratory it has been found advantageous to retain the bromine at C-12 since in the subsequent, modified Meystre–Miescher degradation of the side-chain[6] the desired C-20 ketone is isolated with comparative ease when bromine is present, and only with considerable difficulty when bromine is absent

We have applied Gallagher's approach in such a way that starting with desoxycholic acid, compound IX, an intermediate in the Kendall synthesis, is obtained. The number of steps has been reduced to seven, although our studies have not resulted in better than 10% over-all yield of IX from IV.

3α-Succinoxy-12-ketocholanic acid (IV), which is prepared readily from desoxycholic acid,[7] was brominated with bromine at 60° in glacial acetic acid solution to give a mixture of 11α- and 11β-bromo-3-succinoxy-12-ketocholanic acids (V). This mixture was then refluxed for several hours with a

(1) (a) R. B. Turner, V. R. Mattox, L. L. Engel, B. F. McKenzie and E. C. Kendall, *J. Biol. Chem.*, **166**, 345 (1946); (b) V. R. Mattox and E. C. Kendall, *ibid.*, **185**, 589 (1950); (c) E. C. Kendall, U. S. Patent 2,541,074, Feb. 13, 1951.

(2) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, p. 452.

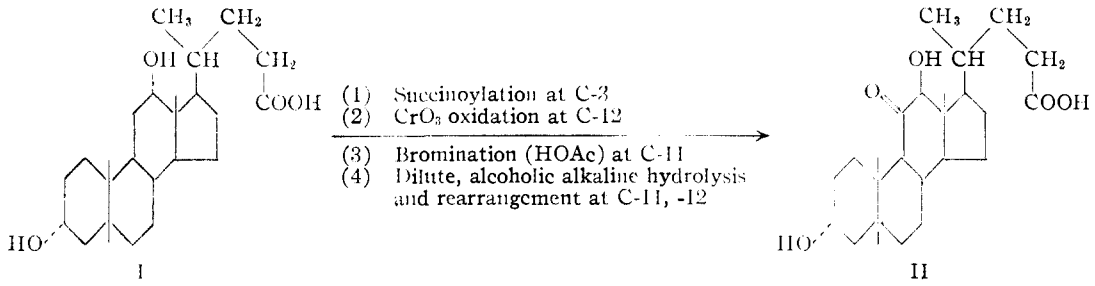
(3) (a) J. von Euw and T. Reichstein, *Helv. Chim. Acta*, **29**, 654 (1946); (b) A. Lardon and T. Reichstein, *ibid.*, **26**, 747 (1943).

(4) (a) T. F. Gallagher and W. P. Long, *J. Biol. Chem.*, **162**, 521 (1946); (b) T. F. Gallagher, *ibid.*, **162**, 539 (1946); (c) E. Borgstrom and T. F. Gallagher, *ibid.*, **177**, 951 (1949).

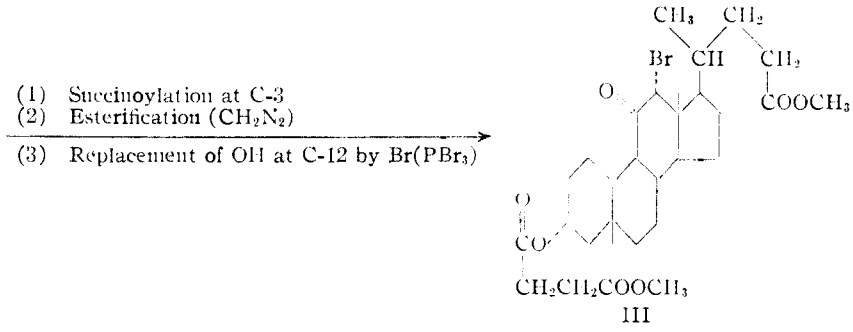
(5) E. P. Kohler and M. Tishler, THIS JOURNAL, **54**, 1594 (1932).

(6) Ch. Meystre and A. Wettstein, *Helv. Chim. Acta*, **30**, 1037 (1947).

(7) E. Schwenk, B. Riegel, R. B. Moffett and E. Stahl, THIS JOURNAL, **65**, 549 (1943).

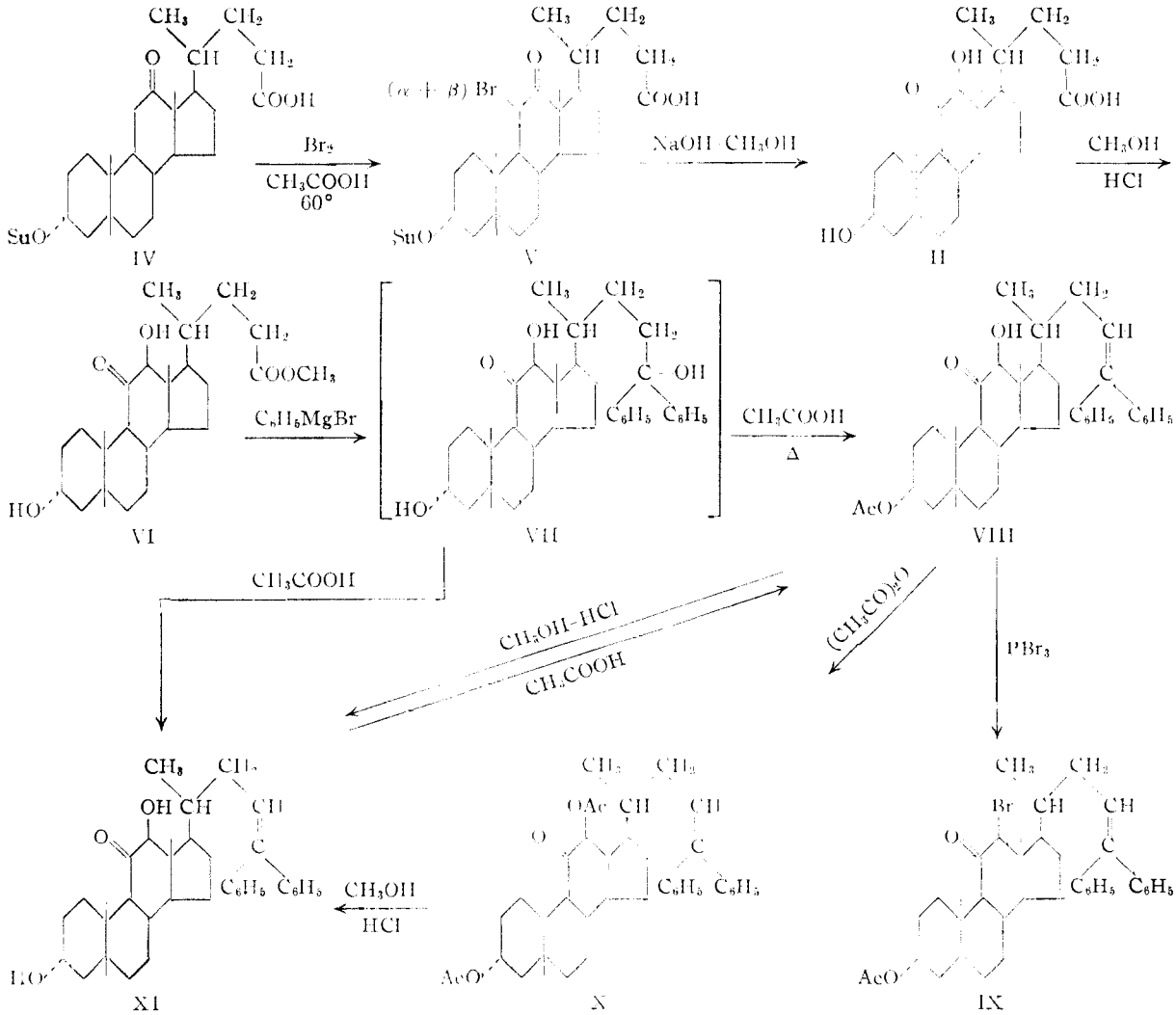


I II



III

Gallagher[4c] studied the isomerization of II in hot alkali, and showed that the resulting mixture consisted of 63% of starting material, 30% of 3α,11α-dihydroxy-12-ketocholanic acid and smaller amounts of the remaining two isomers. They suggested that this mixture represented an equilibrium. We were able to improve the yield of II substantially by isolating and purifying II and then recycling the residues. It was found that one recycle gave a second crop of from one-half to two-thirds as much II as that from the solution of sodium hydroxide in aqueous methanol to effect the rearrangement of the intermediate 11-hydroxy-12-ketone into the 12β-hydroxy-11-ketone (Marker–Lawson acid, II). Borgstrom and



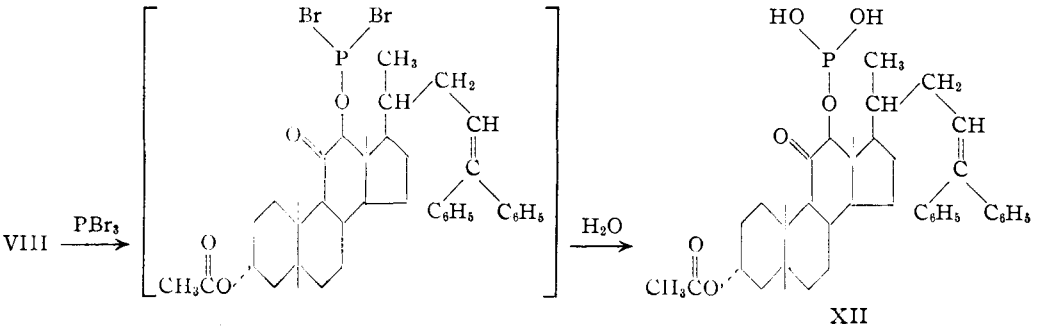
IV V II VI VII VIII XI X IX

first pass, the over-all yield averaging about 60% from IV.

The Marker–Lawson acid (II) was esterified[8] and the ester (VI) was treated with a large excess of phenylmagnesium bromide. By varying the subsequent treatment of the reaction mixture it was possible to obtain VIII or XI. Dehydration of the crude 24-carbinol (VII) by brief refluxing with acetic acid gave XI in 28% yield. Prolonged refluxing with glacial acetic acid resulted in acetylation at C-3 in addition to dehydration of the 24-carbinol to give VIII in 58% yield. The relationships among the three derivatives VIII, X and XI were established by demonstrating their interconvertibility. From XI, VIII was prepared by refluxing with acetic acid. Similarly, VIII was converted to X by refluxing with acetic anhydride. Both VIII and X were converted to XI by transesterification with methanolic hydrogen chloride.

The 3-acetoxydiphenylcholene derivative (VIII) was then converted to IX by treatment with phosphorus tribromide. Although a wide variety of conditions were investigated, the best yield of IX obtained was 32%, which resulted from the interaction of 1.0 to 1.5 moles of phosphorus tribromide per mole of VIII in concentrated methylene chloride solution at room temperature. From many of the experiments aimed to produce IX, a phosphorus-containing substance was isolated, the empirical formula of which corresponded to that of the 12-phosphite ester of VIII (XII).

It was possible to prepare XII in 80–90% yield when two moles of pyridine and 1.2–3.5 moles of phosphorus trichloride were used per mole of VIII. The yield of phosphite decreased when a smaller or larger amount of pyridine was employed. In like fashion the sulfite and phosphate esters of VIII were prepared with the aid of thionyl chloride and phosphorus oxychloride, respectively.



When the 12-phosphite (XII) was heated above 80° in glacial acetic acid–anhydrous hydrogen bromide solution it was cleaved to form IX. The best yield of IX (48%) was observed when XII was refluxed for one hour in 0.28 *N* hydrogen bromide in acetic acid. Unfortunately, IX was found to undergo severe decomposition in the reaction medium required to cleave the phosphite. Lower reaction temperatures resulted in a very slow reaction and lower concentrations of hydrogen bromide in acetic acid were likewise ineffective in improving the yield of IX. Hydrogen chloride gas dissolved in glacial acetic acid did not cleave XII to the 12-chloride, but to VIII. In like fashion, hydrogen bromide in acetic acid regenerated the parent compound, VIII, from its 12-sulfite ester.

(8) B. B. Longwell and O. Wintersteiner, *ibid.*, **62**, 200 (1940).

Experimental[9]

3α,12β-Dihydroxy-11-ketocholanic Acid (II).—3α-Succinoxy-12-ketocholanic acid[7] (IV) (500 g.) was dissolved in 7 l. of acetic acid by warming to 70° with stirring. The temperature of the solution was then lowered to 60° and a solution of 168 g. of bromine in 500 ml. of glacial acetic acid was added, with stirring, at such a rate that the addition was complete in from two to three hours. Stirring was continued for one hour while maintaining the solution temperature at 50–60°. At the end of this period the solution was cooled to room temperature, 22 l. of ice-water was added slowly, with stirring, and the precipitated solid was collected with suction and washed thoroughly with water. There was obtained 580 g. of 11-bromo-3α-succinoxy-12-ketocholanic acid (V), m.p. 178–180°; $[\alpha]^{25}D$ +46° (1% in 95% ethanol).

The bromoketone (V) was dissolved in 5 l. of methanol, a solution of 1.0 kg. of sodium hydroxide in 5.0 l. of water was added, and the resultant solution was refluxed in a nitrogen atmosphere for two hours. It was then poured onto 1.5 kg. of sulfuric acid mixed with 25 kg. of ice, and the precipitated solid was filtered, washed with water and dried. The crude acid, 413 g. (99.5%), m.p. 179–181°, was slurried in 830 ml. of boiling ethyl acetate, cooled to 20° and the crystalline solid which formed was collected with suction; weight 346 g. (83.5%), m.p. 185.4–191.8°. A further recrystallization from 2.5 l. of isopropyl alcohol gave 190 g. (46%) of II, m.p. 199.4–200.6°. Crystallization of a portion of this sample once more from isopropyl alcohol raised the m.p. to 203–204°; $[\alpha]^{25}D$ +65.3° (0.93% in 95% ethanol). Longwell and Wintersteiner[8] report that "3α,11-dihydroxy-12-ketocholanic acid," in reality II, melts at 202°, $[\alpha]^{24}D$ +65.7° (2.5% in 95% ethanol) and when more highly purified melts at 205°, $[\alpha]^{27}D$ +67.1° (1.3% in ethanol).

The mother liquors from the previously described purifications were combined, evaporated to dryness, and the residue was retreated with alkali as already described. From the recycle was obtained 138 g. (33%) of II, m.p. 196–198°. A second recycle of the mother liquors gave only products soluble in ethyl acetate.

Methyl 3α,12β-Dihydroxy-11-ketocholanate (VI).—A suspension of 190 g. of II (m.p. 199.4–200.6°) in 570 ml. of methanol was treated with 10 ml. of acetyl chloride and the mixture was refluxed for one hour. The solution was allowed to stand overnight and the precipitated solid which was collected weighed 168 g. (85.5%), m.p. 153.5–154.5°, lit.[8] m.p. 157°. The mother liquors from this reaction could be recycled through the alkaline isomerization described in the preparation of II to yield additional material.

24,24-Diphenylchol-23-en-3α,12β-diol-11-one 3-Acetate (VIII).—To the Grignard reagent prepared from 58.2 g. of magnesium turnings, 276 ml. of bromobenzene and 900 ml. of anhydrous ether there was added, with stirring, a warm solution of 126 g. of VI in 1.2 l. of dry toluene. The ether was distilled from the reaction simultaneously with the addition of the ester and the mixture was heated to 90° for two hours. It was then cooled, decomposed by the addition of 1

(9) All melting points are corrected; the authors are indebted to Mr. Edwin Connor, Mrs. Thomas Barrella and Mrs. Raymond MacEntire of this Laboratory for the microanalyses and optical data, and to Dr. William Tarpley, Miss Cecelia Vitiello and Miss Betty Blasko for the measurement and interpretation of the infrared spectra.

l. of 30% acetic acid and steam distilled until the removal of biphenyl was complete. The residual oil left after decantation of the water was dissolved in ether and dried. Evaporation of the dried ethereal solution gave an oil, which was refluxed in 1 l. of acetic acid for eight hours. The acetic acid solution was poured into 3 l. of ice-water and the solid which precipitated was filtered and dried. Recrystallization of the dry solid from 1.5 l. of acetonitrile gave 99 g. (58%) of 24,24-diphenylchol-23-en-3α,12β-diol-11-one 3-acetate (VIII), m.p. 165–168°. A purified sample obtained by several additional recrystallizations from acetonitrile melted at 170–171°, $[\alpha]^{22}D$ +76.9° (0.8% in chloroform).

Anal. Calcd. for $C_{38}H_{48}O_4$: C, 80.24; H, 8.51. Found: C, 80.14; H, 8.69.

24,24-Diphenylchol-23-en-3α,12β-diol-11-one (XI) from VII.—The procedure for preparing VIII was followed with the exception that the oil left after the evaporation of the ethereal solution was heated to boiling in 95% acetic acid, cooled immediately, and four volumes of water were added. The precipitate which formed was dried and crystallized from methanol. From 63 g. of VI, with all the other reagents in the same proportions as before, and using 400 ml. of 95% acetic acid in the dehydration of the carbinol, there was obtained 22 g. (28%) of XI, m.p. 121–124°. Recrystallization from methanol then raised the m.p. to 128–129°; $[\alpha]^{25}D$ +79.9° (1% in methanol). All analyses of XI crystallized from methanol indicated one-half molecule of solvent of crystallization. Since no solvent was discovered from which an unsolvated, crystalline sample of XI could be obtained, the analysis of the solvate is reported. The structure of XI was verified by its infrared spectrum which showed characteristic absorptions for hydroxyl (solvent?), 11-carbonyl, phenyl and conjugated phenyl, but none for ester carbonyl, which would be present in the event that either the 3- or 12-hydroxyl groups were acetylated.

Anal. Calcd. for $2C_{36}H_{46}O_3 \cdot CH_4O$: C, 80.77; H, 8.92. Found: C, 80.97, 80.57, 80.57; H, 9.21, 9.21, 9.11.

24,24-Diphenylchol-23-en-3α,12β-diol-11-one Diacetate (X) from VIII.—A solution of 53 g. of VIII in 150 ml. of acetic anhydride was refluxed for one-half hour, treated with Darco, filtered hot and allowed to cool. The crystalline material (X) which formed weighed 38 g. (66.8%), m.p. 180–181.5°. A second crystallization from acetonitrile raised the m.p. to 182.5–183.5°, $[\alpha]^{22}D$ +65.1° (1% in chloroform).

Anal. Calcd. for $C_{40}H_{50}O_5$: C, 78.65; H, 8.25. Found: C, 78.62; H, 8.32.

XI from VIII.—To a solution of 1.0 g. of VIII in 15 ml. of methanol was added 0.3 ml. of acetyl chloride and the solution was allowed to stand at room temperature for 24 hours. Then 25 ml. of methanol was added, the solution was refluxed for one hour and concentrated to 15 ml. Upon cooling XI separated as a crystalline solid, weight 550 mg. (59%), m.p. 124–128°. A mixture m.p. with XI directly from the Grignard reaction showed no depression.

XI from X.—A solution of 5.0 g. of X in 125 ml. of methanol was treated with 1.5 ml. of acetyl chloride, refluxed for one hour, concentrated to 50 ml. and cooled. There was thus obtained 2.4 g. (56%) of XI, m.p. 128–129°. A mixture m.p. with XI directly from the Grignard reaction showed no depression.

VIII from XI.—A solution of 750 mg. of XI in 15 ml. of glacial acetic acid was refluxed for 12 hours. Upon dilution of the cooled reaction mixture with water 780 mg. (96%) of VIII, m.p. 164–165.5°, was precipitated. Recrystallization from acetonitrile gave 600 mg., m.p. 169.5–170.5°. A mixture m.p. with VIII directly from the Grignard reaction showed no depression.

12α-Bromo-24,24-diphenylchol-23-en-3α-ol-11-one Acetate (IX). A.—To a solution of 1.0 g. (0.0018 mole) of VIII in 15 ml. of methylene chloride was added 0.17 ml. (0.0018 mole) of freshly distilled phosphorus tribromide. The reaction mixture was allowed to stand overnight, then washed with ice-water, dried over anhydrous magnesium sulfate and concentrated. The gummy residue was dissolved in a small volume of acetic anhydride and held at 0–5° overnight. Collection of the deposited solid gave 0.24 g. (22%) of IX, m.p. 166–172°. Recrystallization of this material from acetic anhydride raised the m.p. to 175–176°. A mixture m.p. of IX with an authentic sample prepared according to the method of Kendall,[1c] m.p. 177–179°, showed no depression. The infrared spectrum of IX was identical with that of the sample prepared by Kendall's method.

B.—To a solution of 1.0 g. of VIII in 15 ml. of methylene chloride and 0.16 ml. (0.0020 mole) of pyridine was added 0.17 ml. (0.0018 mole) of freshly distilled phosphorus tribromide. The procedure used in A was followed here, and there was formed 0.28 g. (25%) of IX, m.p. 167–172°.

C.—To a solution of 5.0 g. (0.0088 mole) of VIII in 15 ml. of methylene chloride was added 3.5 g. (0.013 mole) of phosphorus tribromide. The reaction mixture was processed as in A to the point of isolation of the gummy residue. The residue was taken up in 10 ml. of 0.28 *N* hydrogen bromide in glacial acetic acid and heated for 50 minutes on the steam-bath in a closed vessel. Precipitation of the product by addition of water followed by filtration, drying and recrystallization from acetic anhydride gave 1.1 g. of IX, m.p. 168–170° and a second crop of 0.7 g., m.p. 165–167° (total yield 32%).

24,24-Diphenylchol-23-en-3α,12β-diol-11-one 3-Acetate 12-Dihydrogen Phosphite (XII).—To a solution of 1.0 g. (0.0018 mole) of VIII in 15 ml. of methylene chloride and 0.3 ml. (0.0037 mole) of pyridine was added 0.18 ml. (0.0021 mole) of phosphorus trichloride, and the mixture was allowed to stand at room temperature overnight. The reaction mixture was treated as described in A under the preparation of IX. Evaporation of the methylene chloride solution left a colorless solid which was triturated with hot acetonitrile. Upon cooling, XII remained as a crystalline solid, weight 0.91 g. (81.5%), m.p. 209.5–211°. The melting point rose to 215–216° after recrystallization from a mixture of methylene chloride–acetonitrile; $[\alpha]^{22}D$ +71.3° (0.63% in chloroform).

Anal. Calcd. for $C_{38}H_{49}O_6P$: C, 72.13; H, 7.81; P, 4.89. Found: C, 72.15; H, 7.90; P, 5.32.

Using 0.4 ml. (0.0049 mole) of pyridine in the preceding experiment a 59% yield of XII, m.p. 207–210°, was obtained, and using 0.6 ml. (0.0074 mole) of pyridine, XII was formed in 28% yield, m.p. 208–210°. The amount of phosphorus trichloride used was not critical between the limits 1.2–3.5 moles per mole of VIII.

IX from XII.—A solution of 500 mg. of XII in 50 ml. of 0.28 *N* hydrogen bromide in glacial acetic acid and 20 ml. of glacial acetic acid was refluxed for one hour, cooled to room temperature and water was added dropwise to turbidity. A precipitate of IX formed upon standing at 0–5° overnight; yield 240 mg. (48%), m.p. 160–166°. Recrystallization from acetic anhydride raised the m.p. to 175–176°. The identity of IX was established as described in A.

An identical result was achieved by heating the same reaction mixture for five hours at 80–85°. Increasing the hydrogen bromide concentration or lengthening the duration of the heating period had an adverse effect on the yield of IX. The same was also true for a decrease in the hydrogen bromide concentration or for a shorter period of heating.

Action of Hydrogen Bromide in Acetic Acid on IX.—A solution of 0.5 g. of IX, m.p. 177–179°, in 50 ml. of 0.28 *N* hydrogen bromide in glacial acetic acid was refluxed for two hours, whereupon the reaction mixture was cooled and its contents precipitated by pouring into water. Recrystallization of the crude product from acetic anhydride gave 0.25 g. of IX, m.p. 158–162°. Repeated crystallization from acetic anhydride raised the m.p. to 173–175°, and a mixture melting point of the starting material with this sample showed no depression.

Action of Hydrogen Chloride in Acetic Acid on XII.—A solution of 0.5 g. of XII in 50 ml. of 0.88 *N* hydrogen chloride in glacial acetic acid and 20 ml. of glacial acetic acid was refluxed for one hour and processed in the usual way. A first crop of 0.29 g., m.p. 166–169.5° was obtained. Its identity with VIII was established by mixture m.p., which showed no depression, and by examination of the infrared spectrum, which was identical with that of an authentic sample of VIII. A second crop (0.15 g.), m.p. 208–211°, was isolated from the mother liquors upon addition of more water. This was found to be unreacted XII.

24,24-Diphenylchol-23-en-3α,12β-diol-11-one 3-Acetate 12-Hydrogen Sulfite.—A solution of 1.0 g. (0.0018 mole) of VIII in 15 ml. of methylene chloride containing 0.15 ml. (0.0019 mole) of pyridine was treated with 0.23 ml. (0.0032 mole) of thionyl chloride. The reaction mixture was allowed to stand overnight and was then washed three times

with cold water, dried and evaporated to dryness *in vacuo*. The residue was crystallized from acetonitrile and two crops were collected, 0.25 g., m.p. 140–141° dec., and 0.1 g., m.p. 136–139° dec.

Anal. Calcd. for $C_{38}H_{48}O_6S$: S, 5.06. Found: S, 4.72.

Using a procedure similar to that described for the preparation of the sulfite, but with phosphorus oxychloride in the place of thionyl chloride, a phosphorus containing substance, m.p. 201–203° dec., was obtained. This was probably the 12-phosphate ester formed by analogy with the esters described previously.

Formation of VIII by the Action of Hydrogen Bromide in Acetic Acid on the Sulfite Ester.—A solution of 200 mg. of sulfite ester in 20 ml. of 0.28 *N* hydrogen bromide in glacial acetic acid was warmed for one minute on the steam-bath, cooled, and 100 ml. of water was added. The resulting precipitate was filtered and crystallized from acetonitrile, giving a crystalline solid, m.p. 165–168°. This substance depressed the melting points of both the sulfite ester and IX. It did not depress the m.p. of VIII, and its infrared spectrum was identical with that of VIII.

BLOOMFIELD, NEW JERSEY RECEIVED NOVEMBER 19, 1951

[CONTRIBUTION FROM THE RESEARCH LABORATORY ATTACHED TO TAKEDA PHARMACEUTICAL INDUSTRIES, LTD.]

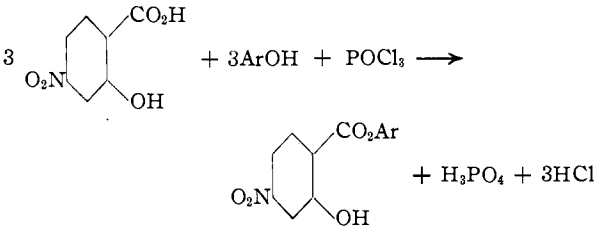
Studies on Antituberculotics. I. Preparation of Aryl *p*-Aminosalicylates

BY SUTTEKITI MARUYAMA AND HISASHI IMAMURA

Several new aryl *p*-aminosalicylates have been prepared for investigation of their use as antituberculotics. Some new derivatives of *p*-aminosalicylic acid have also been prepared. The general methods for their preparation are given.

Freire[1] has recently reported that phenyl *p*-aminosalicylate (I) is about five times as effective as *p*-aminosalicylic acid (PAS) and nearly as effective as streptomycin as an antitubercular agent. However, no description has been made by him of, and no record is present in the literature on, the preparation and the physical and chemical properties of this interesting compound.

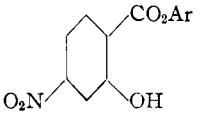
We have prepared I and several other aryl *p*-aminosalicylates as potential antituberculostats. These are listed in Table II. For this purpose, the



a reaction similar to that well-known for the preparation of salol. The use of nitrobenzene (procedure A) was found to be unnecessary for aryl *p*-nitrosalicylates of lower melting points, such as II, III, IV and V. To the nitro-acid esters are common the properties of giving red coloration in dilute alcoholic solution with ferric chloride, of turning red in contact with 1 *N* sodium hydroxide solution, of separating out unchanged from their cold, caustic alkali solution (on carbonation), and of being, unlike free *p*-nitrosalicylic acid, insoluble in 0.1 *N* sodium acetate solution.

TABLE I[d]

ARYL *p*-NITROSALICYLATES



	ArOH	Yield, %	Crystal form; crystallized from	M.p.,[c] °C.	Formula, mol. wt.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I′	Phenol	78[a]	Prisms; methanol	150–151	$C_{13}H_9NO_5$ 259.21	60.23		3.50		5.40	5.51
II′	*p*-Cresol	73[a]	Prisms; methanol	120–122	$C_{14}H_{11}NO_5$ 273.24	61.53	61.26	4.06	4.04	5.13	5.09
III′	*p*-Chloro-*m*-cresol	80[a]	Plates; dil. HAc	120–121	$C_{14}H_{10}NClO_5$ 307.69	54.65	54.61	3.28	3.68	4.55	4.81
IV′	Thymol	76[a]	Prisms; dil. HAc	60–61	$C_{17}H_{17}NO_5$ 315.31	64.75	64.86	5.43	5.75	4.44	4.12
V′	Guaiacol	70[a]	Long prisms; methanol	105–106	$C_{14}H_{11}NO_6$ 289.24	58.13	58.02	3.83	4.85	4.84	4.96
VI′	β-Naphthol	52[b]	Prisms; dil. HAc	188–190	$C_{17}H_{11}NO_5$ 309.27	66.02	66.10	3.59	3.88	4.53	4.55
VII′	*p*-Nitrophenol	[f]	Long prisms; acetic acid[e]	151–152	$C_{13}H_8N_2O_7$ 304.06	51.64	51.47	2.63	2.92	9.15	9.38

[a] Yield of pure product based upon consumed *p*-nitrosalicylic acid. [b] Yield of almost pure product after washing with sodium acetate solution, based upon consumed *p*-nitrosalicylic acid. [c] All melting points are uncorrected values. [d] Analyses were carried out on 3–8-mg. samples (Pregl). [e] Methanol should not be used because of the transesterification which it effects. [f] Not observed.

corresponding nitro compounds, listed in Table I, were first prepared by the reaction of *p*-nitrosalicylic acid[2] with the appropriate phenol with (procedure A) or without nitrobenzene (procedure B) as solvent in the presence of phosphorus oxychloride

(1) S. A. Freire, *Compt. rend.*, **231**, 728, 1004 (1950).

(2) (a) W. Borsche, *Ber.*, **42**, 3956 (1909); (b) W. Borsche, *Ann.*, **390**, 3 (1912); (c) J. F. Meghie and C. Morton, *J. Soc. Chem. Ind.*, **68**, 328 (1949).