(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone and 10 g. of sodium hydroxide in 20 ml. of ethanol and 40 ml. of water was refluxed for two hours. The acid was isolated in the usual way and was recrystallized from methanol. The product (1.4 g.) consisted of colorless cotton, m.p. 210.5–212°.

Anal. Calcd. for $C_{21}H_{22}O_7$: C, 65.27; H, 5.74. Found: C, 65.44; H, 5.81.

The infrared spectrum of this ketoacid ($CHCl_3$) included bands at 5.83 μ (acid carbonyl), 5.96 μ (ketone) and 6.22 μ.

This acid was esterified by refluxing it in a 3% solution of concentrated sulfuric acid in absolute ethanol for four hours. Recrystallization of the neutral product from ether–methanol provided colorless crystals, m.p. 132–133.5°. The mixed m.p. with *trans*-3-carbethoxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone was 132–133.5° (undepressed).

1-(3′,4′-Dimethoxyphenyl)-2-carbethoxy-6,7-dimethoxytetralin (XII).—A solution of 2.1 g. of 3-carbethoxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone in 150 ml. of glacial acetic acid containing 1.0 g. of 5% palladium–charcoal catalyst was shaken at 60° under hydrogen (40 lb.) for two hours. Filtration of the catalyst and evaporation of the acetic acid gave a quantitative yield of crystalline material. Purification was effected by recrystallization from cyclohexane–ether; colorless, cottony crystals, m.p. 97–98°.

Anal. Calcd. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.07; H, 6.90. The infrared spectrum ($CHCl_3$) showed a band at 5.79 μ.

1-(3′,4′-Dimethoxyphenyl)-6,7-dimethoxy-2-carboxytetralin (XIII).—A mixture of 2.7 g. of the ester, XII, and 15 g. of sodium hydroxide in 45 ml. of water and 5 ml. of ethanol was refluxed for two hours. The salt suspension was diluted with 250 ml. of water and was warmed to provide a solution, which was filtered, acidified with hydrochloric acid, and chilled. The crystals were collected, washed with two portions of water, and air dried. Trituration with ether–methanol gave 2.3 g. (85%) of colorless crystals, m.p. 181–183°. Recrystallization from methanol afforded an analytical sample; colorless, fluffy crystals, m.p. 184.5-186.5°.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.95; H, 6.54.

The infrared spectrum of this acid was characterized by a sharp peak at 5.77 μ.

1-(3′,4′-Dimethoxyphenyl)-2-carboxy-6,7-dimethoxynaphthalene (XIV).—A mixture of 0.6 g. of the acid, XIII, 25 ml. of biphenyl, and 1.5 g. of 5% palladium–charcoal catalyst was refluxed vigorously for three hours. Ethyl acetate (500 ml.) was added, after cooling the suspension, and the mixture was filtered to remove the catalyst. The filtrate was extracted with two portions of 5% sodium hydroxide solution. The alkaline extract was acidified with hydrochloric acid, and was chilled. The crystals were collected, washed with water, and air dried. The yield of crude acid was 0.4 g. (66%). Recrystallization from methanol (Norit) gave colorless crystals, m.p. 207.5–210°.

Anal. Calcd. for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.53; H, 5.44.

The ultraviolet absorption spectrum of this naphthalene was measured in ethanol solution. Maxima were observed at 220 mμ (log ε 4.77), 255 mμ (log ε 4.03) and 291 mμ (log ε 3.53). The ultraviolet absorption spectrum of 6,7-dimethoxy-2-carboxynaphthalene[1] in the same solvent had maxima at 215 mμ (log ε 4.20), 247 mμ (log ε 4.78), and 294 mμ (log ε 4.03).

The infrared spectrum ($CHCl_3$) showed broad absorption in the region of 3.0 μ and a band at 5.89 μ.

When *p*-cymene was substituted for biphenyl in the above reaction the starting material was recovered quantitatively.

BETHESDA, MARYLAND

[CONTRIBUTION FROM THE LABORATORY OF CHEMISTRY OF NATURAL PRODUCTS, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, FEDERAL SECURITY AGENCY]

Podophyllotoxin Studies. A Synthesis of the Carbon–Oxygen Skeleton

BY GORDON N. WALKER

RECEIVED JANUARY 23, 1953

Dieckmann cyclization of the required triester gave 2-carbomethoxy-3-carbethoxy-4-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxy-1-tetralone (III). This compound was converted *via* catalytic hydrogenolysis and hydrolysis to a tetralin anhydride, V, and *via* mild hydrolysis and acetylation to an unsaturated acetoxyanhydride, VI. Hydrolysis and decarboxylation of III gave the tetralone-acid, IVa, esterification of which led to the ester, IVb.

Derivatives of 1-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxytetralin, I, have not been obtained frequently by synthetic routes. Haworth and coworkers[1,2] prepared several closely related naphthalenes, and a dihydronaphthalene,[1] and Tarbell[3] reported a product of the reaction of isosafrole with 3,4,5-trimethoxycinnamic acid which was probably a compound having this ring system. This report deals with a new synthesis of compounds derived from I, in particular the ketodiester, III, and with several reactions of III which led to compounds closely related to podophyllotoxin.

The general approach in this synthesis was similar to that followed in obtaining 3-carbethoxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone.[4] A Stobbe condensation of the ketoester, II,[5] with ethyl succinate and potassium *t*-butoxide gave an acid ester. The acid group appeared to be sterically hindered, since an attempt to esterify the material by the Fischer method was not successful. Esterification was effected with diazomethane. The neutral product was hydrogenated in glacial acetic acid at 80° in the presence of a palladium–charcoal catalyst. In this medium little hydrolytic cleavage of the methylenedioxy group occurred, although the absorption of hydrogen was very slow. The neutral material remaining after hydrogenation was subjected to Dieckmann cyclization. The reaction appeared to be accompanied by decomposition, and led to III in low yield. No other compounds were isolated from the crude product of this cyclization, and the stereochemical structure of III was not determined. Structure III was confirmed by the infrared spectrum,[6] in which

---

[1] R. D. Haworth and T. Richardson, *J. Chem. Soc.*, 348 (1936).

[2] R. D. Haworth, T. Richardson and G. Sheldrick, *ibid.*, 1576 (1935).

[3] R. G. Nelb and D. S. Tarbell, THIS JOURNAL, **71**, 2936 (1949).

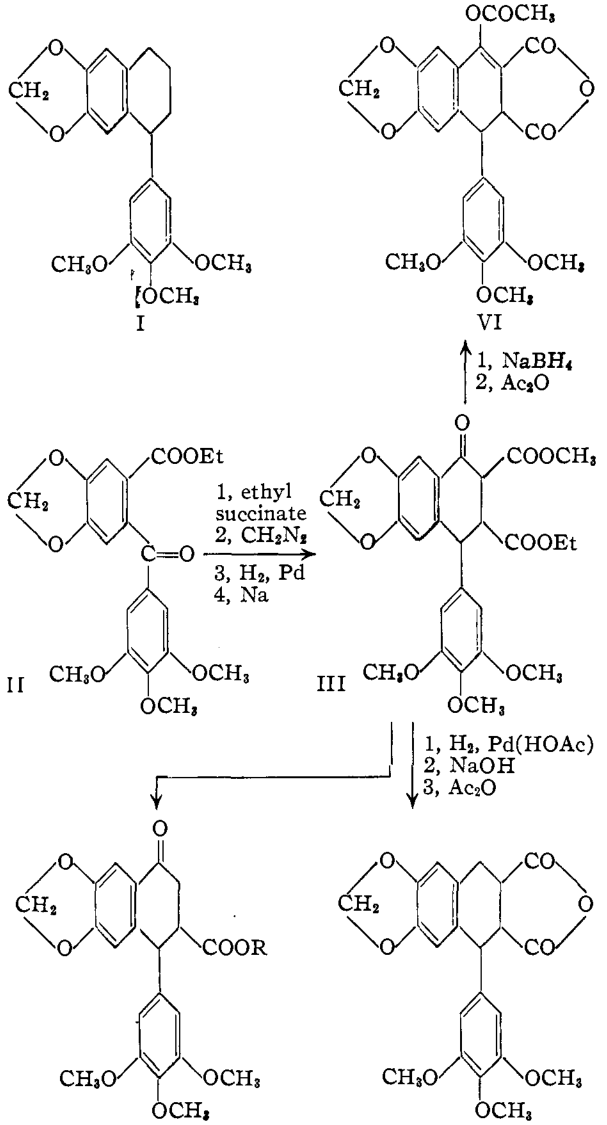
[4] G. N. Walker, *ibid.*, **75**, 3387 (1953).

[5] W. J. Gensler and C. H. Samour, *ibid.*, **73**, 5555 (1951).

[6] For complete infrared spectra for the substances referred to in this article order Document 3924 from ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C., remitting $1.25 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.25 for photoprints readable without optical aid.

there appeared a band at 6.00 μ, indicative of a six-membered conjugated ketone,[4] and a band at 5.78 μ, representing an ester.

Hydrolysis and decarboxylation of III in strong alkali gave the ketoacid, IVa. The corresponding methyl ester, IVb, was prepared from IVa by esterification with diazomethane. The infrared spectra[6] of these compounds were in agreement with the structures shown, and were very similar, respectively, to those of 3-carboxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone and the ethyl ester of that ketoacid.[4]



Hydrogenolysis of III in acetic acid at 80° in the presence of a palladium–charcoal catalyst afforded material which, in turn, was hydrolyzed. The resulting acid was converted directly to the anhydride, V, by treatment with acetic anhydride. Analysis of V indicated that the compound was solvated, but the infrared spectrum showed clearly that a cyclic anhydride was at hand.

In an attempt to reduce the keto group of III selectively, III was treated with sodium borohydride in an aqueous solvent. No reduction occurred, but ester exchange and selective hydrolysis of the 2-carbalkoxy group apparently took place in the mild alkaline environment. An infrared spectrum of the product showed that both a conjugated carbonyl group and a carboxylic acid group were present. Acetylation of the product in acetic anhydride led also to anhydride formation. Structure VI was assigned to the acetylated material on the basis of the infrared spectrum.[6] In the latter, bands at 5.39 and 5.62 μ disclosed the presence of a saturated cyclic anhydride, and a peak at 6.10 μ indicated a double bond conjugated with an aromatic ring.

The fact that VI was obtained from III constitutes a proof of the validity of the tetralin structure, III, since an indanone derivative corresponding in elementary composition to III would be unable to form an enol acetate without at the same time undergoing loss of one carboxyl group. This acetylation, with respect to the retention of the 2-carboxy group during the reaction, resembles an acetylation of 3,4-dimethoxyphenylitaconic acid which was studied earlier.[7] In the latter reaction, α-acetyl-3,4-dimethoxyphenylitaconic anhydride was obtained, rather than a ketoacid.

The stereochemical arrangement of the various groups in IV, V and VI, like that of those in III, is not known.

Acknowledgment.—The author is indebted to Mrs. Iris Siewers and Miss Alice Bernardi of the Instrument Laboratory for the spectra reported in this paper, and to Dr. William C. Alford and his staff for the analytical data.

Experimental[8]

2-(3′,4′,5′-Trimethoxybenzoyl)-piperonylic Acid.—The synthesis of Gensler and Samour,[5] starting from piperonal, was used without modification. The ketoacid, recrystallized from methanol, had m.p. 210–213° (reported[5] m.p. 215.2–215.7°).

Ethyl 2-(3′,4′,5′-Trimethoxybenzoyl)-piperonylate (II).—Esterification of the ketoacid was carried out as usual.[5] The crude ester, after evaporation of the ether, was distilled *in vacuo*. From 46 g. of ketoacid there was obtained 30 g. (61%) of colorless glass, b.p. 245–250° (0.2 mm.). This material did not crystallize (reported[5] m.p. 96.5–97°).

Stobbe Condensation.—To a solution of 8.3 g. (0.213 g. atom) of potassium in 200 ml. of *t*-butyl alcohol was added, while stirring, a solution of 30 g. (0.077 mole) of II and 27 g. (0.212 mole) of ethyl succinate in 200 ml. of *t*-butyl alcohol. The mixture was refluxed and stirred for four hours. The *t*-butyl alcohol was removed completely by distillation *in vacuo* at 100° with stirring. The dark residue was dissolved in 500 ml. of water. The solution was washed with ether, acidified at ice temperature with dilute hydrochloric acid, and allowed to stand in the cold overnight. The product was extracted with ethyl acetate. The ethyl acetate solution was washed with three portions of water and was dried over magnesium sulfate. Evaporation of the solvent afforded 45.2 g. of red, viscous oil. The infrared spectrum (chloroform) had broad bands at 2.85 and 5.8 μ. The ultraviolet spectrum consisted of broad absorption over the range 200–300 mμ; there was an inflection or, in some cases a peak, at 295 mμ (log ε 3.85–3.9). The material was soluble in sodium bicarbonate solution, and did not give an appreciable ferric chloride test.

Esterification.—A solution of the crude Stobbe product (45 g.) in 200 ml. of dry ether was added gradually to a solution of diazomethane, prepared from 30 g. of nitroso-

---

(7) E. C. Horning and G. N. Walker, THIS JOURNAL, **74**, 5147 (1952).

(8) All melting points are corrected.

methylurea, in 800 ml. of dry ether. Brisk evolution of gas occurred. The solution was allowed to stand overnight. The ether was evaporated and the residue was again dissolved in ether. The ether solution was washed with several portions of 5% sodium hydroxide solution, and with successive portions of water, dilute acetic acid, sodium bicarbonate solution and water. After drying the solution (magnesium sulfate) and evaporating the ether there remained 37.4 g. of oil. The infrared and ultraviolet spectra were very similar to those of the Stobbe product.

Hydrogenation.—A mixture of 36 g. (0.068 mole) of the triester, 5 g. of 5% palladium-charcoal catalyst and 200 ml. of glacial acetic acid was shaken at 80° under hydrogen, initially at 40 lb., for nine hours. A pressure drop of 4.7 lb. (representing 0.060 mole) was observed during this period. The catalyst was removed by filtration, and the acetic acid was evaporated. The residue was dissolved in ethyl acetate. The ethyl acetate solution was washed with three portions of 5% sodium hydroxide solution and with successive portions of water, dilute acetic acid, sodium bicarbonate solution and water. It was dried over magnesium sulfate. Evaporation of the solvent gave 31.2 g. of orange oil.

2-Carbomethoxy-3-carbethoxy-4-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxy-1-tetralone (III).—A suspension of 1.7 g. (0.074 g. atom) of sodium and 0.2 g. of potassium in 300 ml. of dry toluene was refluxed and stirred vigorously for a half hour until fine sand was obtained. The heating was discontinued. While continuing to stir the mixture vigorously, there was added a solution of 29 g. of crude hydrogenation product in 100 ml. of dry toluene, over a period of 15 minutes. Heat was evolved, and a very dark suspension was formed. After the initial action subsided, the suspension was refluxed and stirred vigorously for two hours, and was allowed to cool to room temperature while stirring was maintained. After treatment with 10 ml. of methanol (stirring) the solution was diluted with ethyl acetate and washed with several portions of 5% sodium hydroxide solution. The solution was then washed with successive portions of water, dilute acetic acid, sodium bicarbonate solution and water, and was dried over magnesium sulfate. The solvents were evaporated. The crude product, 15.7 g. of black gum, crystallized in part in methanol. The crystals were collected, washed with methanol, and dried *in vacuo;* tan crystals, 3.8 g., m.p. 208–217°, were obtained. Additional material (0.4 g.) crystallized when the filtrates were allowed to stand for a month. The yield of keto-diester was 4.2 g. (11% from II). The crystals were very sparingly soluble in methanol. Purification was effected by recrystallization from methanol-ethyl acetate (Norit); colorless crystals, m.p. 224–228°.

Anal. Calcd. for $C_{25}H_{26}O_{10}$: C, 61.72; H, 5.39. Found: C, 61.86; H, 5.10.

The infrared spectrum (chloroform) showed bands at 5.78 μ (ester) and 6.00 μ (ketone), and a shoulder at 6.08 μ (conjugated enol double bond). The compound was insoluble in 5% sodium hydroxide solution. It gave a green color with ferric chloride. An orange crystalline precipitate was obtained with 2,4-dinitrophenylhydrazine.

3-Carboxy-4-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxy-1-tetralone (IVa).—A solution of 4.4 g. of crude cyclization product and 10.5 g. of sodium hydroxide in 40 ml. of water and 5 ml. of methanol was refluxed for three hours. The solution was cooled, diluted to 200 ml. with water, filtered, washed with ether and acidified at ice temperature with dilute hydrochloric acid. Effervescence was observed during this acidification. After refrigerating the mixture overnight, the gummy product was collected, washed with water, pressed dry, and dissolved in methanol. The solution was allowed to evaporate slowly. The crystals which separated were collected and were washed with a small quantity of methanol. There was obtained 0.7 g. of nearly colorless crystals, m.p. 211–217°. Recrystallization from methanol afforded colorless, voluminous crystals, m.p. 220–223° (dec.), which, after drying at 100° in high vacuum over phosphorus pentoxide, retained solvent.

Anal. Calcd. for $C_{22}H_{24}O_9$: C, 61.10; H, 5.59. Found: C, 60.69; H, 5.02.

The infrared spectrum of this ketoacid (chloroform) had bands at 2.84 μ, 5.82 μ (acid carbonyl) and 5.95 μ (ketone).

3-Carbomethoxy-4-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxy-1-tetralone (IVb).—To a solution of diazomethane (1 g.) in 800 ml. of ether was added 0.6 g. of IVa. The solid dissolved slowly and a gas was evolved. The ether was evaporated, and the residue was dissolved in ethyl acetate. The solution was washed with 5% sodium hydroxide solution and with successive portions of water, dilute acetic acid, sodium bicarbonate solution and water. It was dried (magnesium sulfate), and the solvent was evaporated. There was obtained 0.6 g. of gummy crystals. Recrystallization from methanol afforded colorless crystals, m.p. 173–175°.

Anal. Calcd. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35. Found: C, 63.82; H, 5.20.

The infrared spectrum (chloroform) of this ketoester included bands at 5.75 μ (ester carbonyl) and 5.96 μ (ketone).

2,3-Dicarboxy-1-(3′,4′,5′-trimethoxyphenyl)-6,7-methylenedioxytetralin Anhydride (V). (A) **Hydrogenation.**—A mixture of 1.4 g. of III, 1.5 g. of 5% palladium-charcoal catalyst and 150 ml. of glacial acetic acid was shaken at 80° under hydrogen (40 lb.) for two hours. The mixture was filtered. The solution was treated with 1.5 g. of fresh catalyst and was hydrogenated again under the same conditions for an additional two hours. The mixture was filtered again, and the acetic acid was evaporated. The product, 1.4 g., was a colorless, viscous oil.

(B) **Hydrolysis.**—The oil from (A) was refluxed with 10 g. of sodium hydroxide in 50 ml. of water for four hours. The resulting solution was diluted to 200 ml., filtered, and acidified in the cold with dilute hydrochloric acid. The mixture was chilled overnight; the crystals were collected, washed with water, and air-dried. The crude yield was 1.1 g. The material became glassy when treated with methanol or ether.

(C) **Anhydrization.**—The crude acid from (B) was treated with 50 ml. of acetic anhydride. The solution was refluxed for two hours, and most of the excess reagent was evaporated. The residue crystallized readily in ethyl acetate. Trituration with this solvent afforded 0.4 g. (33% from III) of crystals, m.p. 214.5–216°. Recrystallization from ethyl acetate gave colorless crystals, m.p. 215–217°, containing solvent of crystallization. Analysis indicated that the solvent retained was acetic acid, although bands representing this material could not be detected with certainty in the infrared spectrum.

Anal. Calcd. for $C_{23}H_{22}O_9$: C, 62.44; H, 5.01. Found: C, 62.21; H, 5.19.

The infrared spectrum (chloroform) had peaks at 5.38 and 5.61 μ (anhydride). The compound was insoluble in sodium bicarbonate solution and slowly soluble in 5% sodium hydroxide solution.

1-(3′,4′,5′-Trimethoxyphenyl)-2,3-dicarboxy-4-acetoxy-6,7-methylenedioxy-1,2-dihydronaphthalene Anhydride (IV). (A) **Attempted Sodium Borohydride Reduction.**—To a suspension of 1.5 g. of III in 30 ml. of water and 40 ml. of methanol was added 3 g. of sodium borohydride in portions. When frothing was completed and the material had dissolved, the solution was refluxed for three hours. Water was added (30 ml.) and the methanol was distilled. The solution was diluted to 400 ml., was washed with ethyl acetate, and was acidified at ice temperature with a solution of 15 ml. of hydrochloric acid in 30 ml. of water. Crystallization occurred when the acidic solution was kept cold for several hours. The crystals were collected, washed with cold water, and air-dried. The crude yield was 1.2 g. Recrystallization from methanol afforded colorless crystals which decomposed gradually above 200°. The infrared spectrum (chloroform) had a broad band in the region 2.8–3.2 μ, a peak at 5.77 μ (ester, acid), and a peak at 6.0–6.05 μ (ketone). This spectrum, together with the analysis, indicated that the compound was a keto-acid-ester, and that ester exchange occurred during the reaction.

Anal. Calcd. for $C_{23}H_{22}O_{10}$: C, 60.26; H, 4.95. Found: C, 60.40; H, 4.89.

The crystals were readily soluble in sodium bicarbonate solution and gave a green color with ferric chloride.

(B) **Reaction with Acetic Anhydride.**—A solution of 1.0 g. of product (A) in 50 ml. of acetic anhydride and one drop of pyridine was refluxed for three hours. Evaporation of the excess reagent gave discolored yellow crystals. Trituration of these with methanol afforded 0.8 g. of product. Recrystallization from ethyl acetate gave yellow crystals, m.p. 274–276° (Kofler hot stage).

Anal. Calcd. for $C_{24}H_{20}O_{10}$: C, 61.54; H, 4.30. Found: C, 61.61; H, 4.25.

The infrared spectrum (chloroform) had peaks at 5.39 and 5.62 μ (anhydride) and at 6.10 μ (conjugated double bond); a shoulder was present at 5.70 μ (enol ester). The infrared spectrum of 3,4-dimethoxyphenylitaconic anhydride[7] was obtained for comparison; it had peaks at 5.42, 5.64 and 6.06 μ (chloroform).

The compound was slowly soluble in 5% sodium hydroxide solution and insoluble in sodium bicarbonate solution.

BETHESDA 14, MARYLAND

[CONTRIBUTION FROM THE LABORATORY ON CHEMISTRY OF NATURAL PRODUCTS, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, FEDERAL SECURITY AGENCY]

Podophyllotoxin Studies. Reductive Methods in the Synthesis of Tetralin Lactones from α-Tetralone Derivatives

BY GORDON N. WALKER

RECEIVED OCTOBER 31, 1952

2-Hydroxymethylene-3-carbethoxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralone (V) was prepared. Catalytic hydrogenolysis of this compound and the corresponding acid (VII) led, respectively, to 1-(3′,4′-dimethoxyphenyl)-2-carbethoxy-3-methyl-6,7-dimethoxytetralin (VIII) and the corresponding acid (IX) while sodium borohydride reduction of V gave 2-hydroxymethyl-3-carboxy-4-(3′,4′-dimethoxyphenyl)-6,7-dimethoxy-1-tetralol (XIII), a tetramethoxy analog of podophyllic acid. From XIII, three lactones, XIV, XV and XVI, were prepared by dehydration under various conditions. A fourth lactone, IV, in the 3′,4′-dimethoxyphenyltetralin series was prepared both *via* sodium borohydride reduction of I and by catalytic hydrogenation of II. The ethylene acetal (X) of V was transformed by sodium borohydride reduction and hydrolysis into a dihydrocarbethoxynaphthaldehyde (XII).

A preceding paper[1] described the preparation of the ketoester, I, together with proof of the tetralone structure for this compound and evidence that the 3-carbethoxy group and the 4-(3′,4′-dimethoxyphenyl) group were disposed in a *trans* configuration in the B-ring. The present report deals with catalytic hydrogenolysis and sodium borohydride reduction of this ketoester and of a hydroxymethylene derivative, V, prepared from it. Certain products of these reactions are close analogs of compounds in the podophyllotoxin series.

Compound V, a crystalline enol, was obtained in high yield when I was treated with ethyl formate in the presence of sodium methoxide. In view of its chemical properties there is no question that V has a keto–enol formula as shown, rather than a naphthalenic structure. It is enolic, as indicated by a ferric chloride test, and it reacts with 2,4-dinitrophenylhydrazine in two stages. Hydrolysis under alkaline conditions is extremely easy and leads to an enolic acid, VII. Chemical and catalytic reductions of V and VII gave products (VI, VIII, IX and XIII) which could be explained best by assuming that V and VII are carbonyl, rather than naphtholic, compounds. These reactions are discussed in detail below. The infrared spectrum[2] of V is unusual inasmuch as no band is present which can be assigned to an enolic hydroxyl group, although a peak at 6.08 μ, representing either a conjugated double bond or a conjugated carbonyl group, is observed, as well as another peak (5.76 μ) representing the carbonyl moiety of an unconjugated ester. The latter is common to the spectra of all 3-carbethoxy tetralins and tetralones which were studied. The spectrum indicates that chelation between the groups at positions 1 and 2 in V is present, resulting in damping of their individual vibrations. An infrared spectrum of hydroxymethylenecyclohexanone indicates that the same phenomenon takes place to a lesser degree in that compound. The infrared spectrum of the enolacid, VII, is similar to that of V except that a very weak band at 6.00 μ, probably due to the conjugated carbonyl group, is also present.

Because of the behaviors of V and VII in catalytic reduction, it is possible that a structure such as V(b) represents these compounds more accurately than does V(a) from the point of view of chemical reactivity. Hydrogenolysis of V in acetic acid at 80° in the presence of a palladium–carbon catalyst involves both oxygen atoms of the keto–enol system and leads to the ester, VIII. This reaction may be explained by assuming that there occurs a stepwise transformation of V(b) in which the aldehyde group, now in a conjugate relationship to the aromatic ring, is affected first. The hydrogenolysis of V could not be carried out stepwise by operating at a lower temperature.

Hydrolysis of VIII in aqueous ethanol leads to the acid, IX, in solvated form. The same acid is obtained in a non-solvated form but in lower yield by hydrogenolysis of the enolacid, VII. Attempts to prepare a lactone directly from VII by partial hydrogenation were not successful.

With ethylene glycol, the hydroxymethylene ketoester, V, forms a mono ethylene acetal, X. Structure X was assigned to the material on the basis of its infrared spectrum, which indicates that a conjugated ketone is present. That the carbonyl group of X is highly hindered is indicated by the extreme slowness with which X reacts with 2,4-dinitrophenylhydrazine. In spite of this fact, reduction with sodium borohydride converts X readily to the corresponding alcohol, XI. The presence in XI of a hydroxyl group is shown clearly through its infrared spectrum. Hydrolysis of the ethylene acetal function in XI under mild acid conditions is accompanied seemingly by elimination of the hydroxyl group. The product, which could

---

(1) G. N. Walker, THIS JOURNAL, **75**, 3387 (1953).

(2) Copies of the full infrared spectra discussed in this paper can be obtained as Document 3858 from the American Documentation Institute, c/o Library of Congress, Washington 25, D. C., remitting $1.25 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.25 for photostats readable without optical aid.