acid (v./v.) was refluxed for 30 min. Water was added to the cooled solution and it was allowed to stand overnight at 5°. The product was filtered and washed with water to afford 68 mg. of the dione IIIa, m.p. 222.5–225.5°. Recrystallization from acetone–petroleum ether gave 56 mg., m.p. 225–228°. One additional crystallization from the same solvent pair did not alter the melting point; λ_{max} 283.5 mμ (ε 26,800); $[\alpha]_D$ +88° (*c*, 0.614). The infrared spectrum was identical to that of the sample prepared above.

21-Acetoxy-17α-hydroxy-4,6-pregnadiene-3,20-dione (IIIb). A mixture of the 7α-hydroxy-21-acetate IIb (0.3 g.), benzene (125 ml.), ethylene glycol (8 ml.), and *p*-toluenesulfonic acid (25 mg.) was refluxed and stirred for 5 hr. with constant water removal. The mixture was cooled, neutralized with sodium bicarbonate, and extracted with chloroform. The extract was washed with saturated saline, dried, and evaporated. The crystalline residue was recrystallized from acetone–petroleum ether to give 240 mg. (83%) of IIIb, m.p. 219–221°; λ_{max} 283 mμ (ε 29,000). Further crystallization raised the m.p. to 223.5–224.5°[14]; ν_{max} 3484, 1757, 1650, 1623, 1592, 1236, and 1095 cm.$^{-1}$.

7α-Hydroxy-4-androstene-3,17-dione (IV). A solution of IIa (0.5 g.) in glacial acetic acid (50 ml.) was shaken with sodium bismuthate (5 g.) for 25 min. After the addition of water, a solution of potassium hydroxide (35 g.) in water (30 ml.) was added, and the mixture was finally neutralized with solid sodium bicarbonate. The product was extracted with chloroform, and the extract was washed once with saturated sodium bicarbonate solution, and three times with saturated saline, dried, and evaporated. The residue was crystallized from acetone–petroleum ether to furnish 107 mg. of crude IV, m.p. 214–215°. Further recrystallization raised the m.p. to 220–222.5°; λ_{max} 241–242 mμ (ε 16,800); ν_{max} 3390, 1748, 1652, and 1087 cm.$^{-1}$; $[\alpha]_D$ +178° (*c*, 1.205), $[M]_D$ +537.

Anal. Calcd. for $C_{19}H_{26}O_3$ (302.40): C, 75.46; H, 8.67. Found: C, 75.71; H, 8.91.

21-Acetoxy-3,20-bisethylenedioxy-5-pregnene-7α,17α-diol (VII). A mixture of the bisethylene ketal of Reichstein's substance S acetate (V, 1.0 g.), *N*-bromosuccinimide (0.46 g.) and anhydrous potassium carbonate (0.2 g.) in carbon tetrachloride (30 ml.) and petroleum ether (b.p. 62–64°) (10 ml.) was refluxed and irradiated for 4 min. by the heat and light of a photospot lamp (Type RSP-2A, General Electric Co.). The filtered solution was stirred at room temperature for 2 hr. with ethyl acetate washed alumina (8 g.), filtered, and evaporated to a glass which was crystallized from ether–petroleum ether to afford 167 mg. of material having a negative Beilstein test, m.p. below 110°; λ_{max} 241 and 285 mμ. The alumina was stirred for 20 min. with approximately 150 ml. of acetone, filtered, and evaporated to a white crystalline solid. Crystallization of the residue from acetone–petroleum ether gave 433 mg. of product, m.p. 193.5–196° with previous softening. Four additional crystallizations from the same solvent pair afforded 190 mg. of the pure diol VII, m.p. 201.5–203.5°; λ_{max} none; ν_{max}^{Nujol} 3550, 3450, 1755, 1680, 1265, 1245, and 1103 cm.$^{-1}$; $[\alpha]_D$ −71° (*c*, 0.973).

Anal. Calcd. for $C_{27}H_{40}O_8$ (492.59): C, 65.83; H, 8.19. Found: C, 65.75; H, 8.12.

21-Acetoxy-3,20-bisethylenedioxy-17α-hydroxy-5-pregnen-7-one (VIII). *A.* A solution of 240 mg. of VII (obtained by evaporation of the mother liquors of the preceding experiment) in 10 ml. of pyridine was added to a slurry of 170 mg. of chromic anhydride in 17 ml. of cold pyridine. After standing at room temperature for 16 hr., the reaction mixture was poured into ice water and extracted with ethyl acetate. The extract was washed with 10% acetic acid (v./v.) and with water, dried, and evaporated. The residue was crystallized from ether–petroleum ether to afford 130 mg. of product, m.p. 185–186.5°; λ_{max} 240 mμ (ε 12,700). Recrystallization from ether–petroleum ether gave 98 mg., m.p. 186–187.5°. Two additional crystallizations from the same solvent pair did not alter the melting point; λ_{max} 240 mμ (ε 13,000); ν_{max}^{Nujol} 3650, 1761, 1683, 1642, 1242, and 1093 cm.$^{-1}$; $[\alpha]_D$ −63° (*c*, 0.590).

Anal. Calcd. for $C_{27}H_{38}O_8$ (490.57): C, 66.10; H, 7.81. Found: C, 66.43; H, 7.96.

B. In another run, the 7α-hydroxy-bis-ketal VII (685 mg.) was oxidized in the same manner as above and the residue obtained from a benzene extract was crystallized from acetone–ether–petroleum ether to afford 495 mg. of product, m.p. 183–185°. An additional 74 mg., m.p. 179–182°, was obtained by concentration of the mother liquor to bring the total yield to 83%.

21-Acetoxy-20-ethylenedioxy-17α-hydroxy-4,6-pregnadien-3-one (IX). In an attempt to salvage more of the 7-keto analog VIII, several mother liquors from the alumina hydrolysis of the 7α-bromo compound VI were evaporated and the residue (3.8 g.) was oxidized in the same manner as above. The benzene extract was evaporated and the oily residue was treated with acetone–ether–petroleum ether to give a semisolid. After decanting the supernatant liquid, the semisolid residue was triturated with ether to afford 0.22 g. of solid, m.p. 183–187°. Addition of petroleum ether to the decantate precipitated 0.50 g. which was recrystallized from acetone–petroleum ether to give 0.35 g., m.p. 182.5–187.5°. The latter fraction was combined with the above 0.22 g. and recrystallized from acetone–petroleum ether to afford 0.33 g., m.p. 184–189.5°; ν_{max}^{Nujol} 3550, 1737, 1682, 1633, 1600, and 1102 cm.$^{-1}$ One recrystallization from ether–petroleum ether, one from aqueous methanol and two from acetone–petroleum ether gave 0.18 g. of the 4,6-diene-3-one IX, m.p. 191.5–194°; λ_{max} 283–284 mμ (ε 25,100); $[\alpha]_D$ +39° (*c*, 0.536).

Anal. Calcd. for $C_{25}H_{34}O_6$(430.52): C, 69.74; H, 7.96. Found: C, 68.49, 68.82; H, 7.75, 7.97.

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[14] Ref. 3 gives m.p. 220–222°, λ_{max} 284 mμ, log ε 4.47 (95% ethanol).

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p-Thiolcinnamic Acid and S-Acyloxy Derivatives[1]

C. G. OVERBERGER, H. BILETCH,[2] AND F. W. ORTTUNG[3]

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During work relating to the preparation of poly-*p*-thiolstyrene by Overberger and Lebovits,[4] *p*-

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[1] This note comprises portions of the Ph.D. dissertation of H. Biletch, Polytechnic Institute of Brooklyn, 1953, and of a thesis submitted by F. W. Orttung in partial fulfillment of the requirements for the degree of Master of Science in the Graduate School of the Polytechnic Institute of Brooklyn, June 1959.

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[3] Present address: Bakelite Co., U. C. C., Research Laboratories, Bound Brook, N. J.

[4] C. G. Overberger and A. Lebovits, *J. Am. Chem. Soc.*, **77**, 3675 (1955); **78**, 4792 (1956).

thiolcinnamic acid and three *p*-thioacyloxycinnamic acids were prepared.

The thiol acid (m.p. 288–290° dec.) was obtained nearly quantitatively by reducing *p*-chlorosulfocinnamic acid[5] with stannous chloride and hydrogen chloride in acetic acid. Reduction of *p*-chlorosulfocinnamic acid with zinc and acetic acid gave a low yield, while zinc and sulfuric acid appeared to attack the double bond as well. Low yields and less pure products also resulted from many other attempts to prepare the thiol acid from either *p*-iodocinnamic acid or diazotized *p*-aminocinnamic acid. Some of these experiments gave a lower melting (210–211°) product which was apparently the *cis* isomer but which was not fully characterized.

Acylation of the thiol group of *p*-thiolcinnamic acid required different conditions for each of three compounds prepared. *p*-Thioacetoxycinnamic acid was obtained in good yield by the action of a tenfold excess of acetic anhydride in either pyridine at reflux or aqueous potassium hydroxide at room temperature, but the use of acetyl chloride failed. However, benzoyl chloride in aqueous potassium hydroxide did yield *p*-thiobenzyloxycinnamic acid. Myristoyl chloride gave no product in aqueous potassium hydroxide, but in pyridine at room temperature a fair yield of *p*-thiomyristoxycinnamic acid was obtained.

Attempted decarboxylations of the *p*-thioacyloxycinnamic acids under a variety of conditions (Cu, Cu-quinoline, $CuSO_4$-quinoline, aq. HBr) gave in some cases evidence of formation of the desired *p*-thiolacyloxystyrenes, but pure monomeric compounds were never obtained.

EXPERIMENTAL[6,7]

***p*-Chlorosulfocinnamic acid.** A solution of 5.0 g. (0.034 mole) of cinnamic acid in 30 g. (0.264 mole) of chlorosulfonic acid was held at 55° for 30 min., cooled, and poured onto 500 g. of cracked ice. The white precipitate was collected and recrystallized from glacial acetic acid, yielding 5.4 g. (66%) of product, m.p. 221–224° dec. A second recrystallization gave 4.8 g. of white flakes, m.p. 224–225° (226°, no yield given).[5]

***p*-Thiolcinnamic acid.** 1. *Reduction of p-chlorosulfocinnamic acid.*

(a) *Stannous chloride–hydrochloric acid.* This procedure is a convenient modification of a general procedure described by Bogert and Bartlett.[8] *p*-Chlorosulfocinnamic acid, 10.0 g. (0.0404 mole) was dissolved in 300 ml. of boiling glacial acetic acid and the solution, after cooling to 75°, was mixed with a solution of 45 g. (0.200 mole) of stannous chloride decahydrate in 40 ml. (0.480 mole) of concentrated hydrochloric acid. The reaction mixture was shaken for 30 min., periodically allowing the escape of gas and then poured into 1000 ml. of water containing 50 ml. of conc. hydrochloric acid. The yellow precipitate was collected, washed free of acid, and vacuum-dried. The product was extremely insoluble but could be recrystallized from acetone after several hours of Soxhlet extraction to effect solution, m.p. 277–280° (dec.). Additional recrystallization yielded 6.9 g. (96%) of yellow powder, m.p. 288–290° (dec.).

Anal. Calcd. for $C_9H_8O_2S$: C, 59.98; H, 4.47; S, 17.79. Found: C, 60.04; H, 4.34; S, 17.69.

(b) *Zinc–sulfuric acid.* Cracked ice (20 g.) and 3.7 ml. of concentrated sulfuric acid were mixed at −5°, and 1.7 g. (0.0068 mole) of *p*-chlorosulfocinnamic acid was introduced slowly during 30 min., after which 2.4 g. (0.037 mole) of zinc dust was added during an additional 30 min. without allowing the temperature to exceed 0°. The system was allowed to warm slowly and was then refluxed for 3 hr. Filtration and recrystallization from acetone as above gave 0.3 g. (26%) of yellow powder, m.p. 277–280° dec.; a mixed melting point with the *p*-thiolcinnamic acid prepared by the first reduction, m.p. 277–280° (dec.) melted at 277–280° (dec.).

When 7 instead of 3 hr. heating was allowed, as recommended by Adams and Marvel[9] for the reduction of benzenesulfonyl chloride, the only product was a small amount of white plates of *p*-thioldihydrocinnamic acid, m.p. 119–120° after two recrystallizations from a methylene chloride–ligroin mixture.

Anal. Calcd. for $C_9H_{10}O_2S$: C, 59.31; H, 5.53; S, 17.59. Found: C, 59.25; H, 5.58; S, 17.73.

(c) *Zinc–Acetic acid. p*-Chlorosulfocinnamic acid, 3.4 g. (0.014 mole), in a mixture of 16 ml. of glacial acetic acid and 40 ml. of water, was stirred at room temperature and treated with 5.0 g. (0.077 mole) of zinc dust added in portions during 15 min. After stirring for 2 hr. and refluxing for 6, a yellow solid was obtained upon dilution with water. Successive washings with methylene chloride and hot acetone gave extracts which, on concentrating, gave, respectively, 0.04 g. of a solid, m.p. 216–220° and 0.32 g. (13%) of yellow powder, m.p. 277–281° (dec.); a mixed melting point with a sample of *p*-thiolcinnamic acid prepared above, m.p. 277–280° (dec.) melted at 277–280° (dec.). The residue after both extractions gave an additional 0.22 g. (9%) of product.

2. *Reaction of potassium ethyl xanthate with diazotized p-aminocinnamic acid. p*-Aminocinnamic acid,[10] 1.63 g. (0.010 mole) was dissolved in 5 ml. of water and 2 ml. of concentrated hydrochloric acid, treated at 0° with 0.7 g. of sodium nitrite and then neutralized to Congo Red with sodium carbonate as described in the procedure of Tarbell and McCall[11] for introducing the sulfhydryl group of 3,5-dichlorothiosalicylic acid. A small amount of excess sodium carbonate was then added and the cold solution was added dropwise during 15 min. to a rapidly stirred solution of 2.57 g. (0.016 mole) of potassium ethyl xanthate in 10 ml. of water kept at 65–70° during the addition and raised to 85° for 15 min. after the addition. Sodium hydroxide solution (2.5 g. in 20 ml. of water) was added and the red solution refluxed under nitrogen for 4 hr. Aqueous hydrochloric acid (1:1) was added until the thick yellow slurry was acid to Congo Red. The solids were filtered off, redispersed in warm dilute hydrochloric acid and treated with a few granules of zinc. When the zinc had disappeared the yellow solids were again filtered, washed, and dried, yielding 0.62 g. (30%) of a fine yellow powder, m.p. 285–287° identical to the previous product prepared by reduction—its ultraviolet spectrum in methanol showed $\lambda_{max} = 296$ mμ, log $\epsilon = 4.23$.

***p*-Thioacetoxycinnamic acid.** *p*-Thiolcinnamic acid, 7.2 g. (0.040 mole) in 200 ml. of 20% aqueous potassium hydroxide

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(5) J. Stewart, *J. Chem. Soc.*, 2555 (1922).

(6) Analyses were performed by Dr. F. Schwarzkopf, Elmhurst, N. Y., and Drs. Weiler and Strauss, Oxford, England.

(7) All melting points are corrected.

(8) M. T. Bogert and J. H. Bartlett, *J. Am. Chem. Soc.*, **53**, 4046 (1931).

(9) R. Adams and C. S. Marvel, *Org. Syntheses*, **Coll. Vol. I**, 504 (1948).

(10) E. R. Blout and D. C. Silverman, *J. Am. Chem. Soc.*, **66**, 1442 (1944).

(11) D. S. Tarbell and M. A. McCall, *J. Am. Chem. Soc.*, **74**, 48 (1952).

was treated with 35 g. (0.343 mole) of acetic anhydride, added portionwise while vigorously shaking and cooling to keep the temperature below 40°. Precipitation was completed by adding 50 ml. of 6*N* hydrochloric acid. The solids were removed by filtration, dried and taken up in 500 ml. of hot methanol. After filtering off inorganic salts and cooling, 5.8 g. of yellow needles were obtained, m.p. 216–217.5°; concentration of their filtrate to 50 ml. yielded an additional 1.9 g. Recrystallization of these combined crops from methanol gave 6.7 g. (75%) of small yellow needles, m.p. 218–219°.

Anal. Calcd. for $C_{11}H_{10}O_3S$: C, 59.44; H, 4.53; S, 14.43. Found: C, 59.68; H, 4.46; S, 14.16.

p-Thiomyristoxycinnamic acid. p-Thiolcinnamic acid, 11.8 g. (0.066 mole) and 1 g. of potassium hydroxide were dissolved in 200 ml. of dry pyridine and the reaction mixture was stirred for 1 hr. Myristoyl chloride, 22.7 g. (0.092 mole) was added dropwise during 1 hr. below 30°, and stirring was continued for 3 additional hr. The solids obtained upon dilution with 500 ml. of water and 100 ml. of 6*N* hydrochloric acid were removed by filtration and then shaken with 200 ml. methanol to remove excess myristic acid. The residue was recrystallized from benzene with the aid of charcoal, 6.8 g. (27%) light yellow plates, m.p. 166–167°.

Anal. Calcd. for $C_{23}H_{34}O_3S$: C, 70.70; H, 8.77; S, 8.21. Found: C, 70.55; H, 8.88; S, 8.00.

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Structure of the Side Chain of Cucurbitacin B

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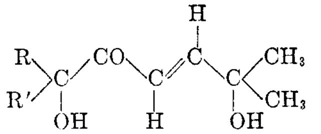
In two recent Communications,[1,2] Lavie and his co-workers have proposed the partial structure I

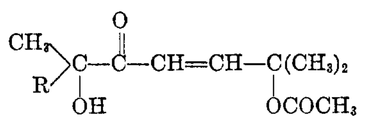


I

$RCH(CH_3)COCH{=}CHC(OH)(CH_3)_2$

II

for elatericin A and α-elaterin. Structure II was proposed by Rivett and Enslin[3] for elaterin and for cucurbitacins A and C. Still more recently[4] partial structure III has been proposed for elaterin



III

and cucurbitacins A, B, and C. From our work we also have concluded that curcurbitacin B (formerly called fabacein II[5]) has structure III, and we wish to report results which confirm this structure and which clarify the results of catalytic hydrogenation.

Cucurbitacin B has been assigned the molecular formula $C_{32}H_{48}O_8$[6] and is a monoacetate, containing an α,β-unsaturated carbonyl group.[5,7] Analyses of an apparently identical product isolated from the juice of *Echinocystis fabacea* were reported[5,8] to agree with the formulas $C_{30}H_{44-46}O_8$ (Calcd. for $C_{30}H_{44}O_8$: C, 67.64; H, 8.33; for $C_{30}H_{46}O_8$: C, 67.39; H, 8.67. Found: C, 67.38; H, 8.40; average of 12 analyses). However the formulas $C_{32}H_{46-48}O_8 \cdot 0.5\ H_2O$ (Calcd.: C, 67.70; H, 8.34; or C, 67.46; H, 8.67) also are equally satisfactory and agree better with the analyses of derived products.

When cucurbitacin B was hydrogenated in 95% ethanol using 10% palladium on carbon as catalyst, from 1.3 to 1.6 moles of hydrogen was absorbed.[8] The resulting solution contained acetic acid, and titration indicated that 0.3 to 0.6 mole of acetic acid was formed. Evidently hydrogenolysis as well as hydrogenation had occurred. The paper chromatogram of the hydrogenated material showed that two products were present which could be separated readily. One product is dihydrocucurbitacin B (VI) (Calcd. for $C_{32}H_{48}O_8$: C, 68.54; H, 8.63; for $C_{32}H_{50}O_8$: C, 68.30; H, 8.96. Found: C, 68.38; H, 8.80); m.p. 163–164° from acetone-hexane; $[\alpha]_D^{25}$ +57° (c = 0.91 in $CHCl_3$); UV (ethanol) λ_{max} 282 mμ, log ε 2.32; IR ($CHCl_3$): 2.92 (OH), 5.79 w(AcO), 5.85 sh (C=O), 5.89 (C=O), 8.10 (AcO). The other product is dihydrodeacetoxycucurbitacin B (VII) (Calcd. for $C_{30}H_{46}O_6$: C, 71.68; H, 9.22; for $C_{30}H_{48}O_6$: C, 71.39; H, 9.59. Found: C, 71.59; H, 9.37); m.p. 208–210° from ether; $[\alpha]_D^{25}$ +57° (c = 0.93 in $CHCl_3$); UV (ethanol) λ_{max} 279 mμ, log ε 2.46; IR ($CHCl_3$): 2.92 (OH), 5.85 sh (C=O), 5.90 (C=O). In both products the α,β-unsaturated carbonyl system present in cucurbitacin B[5,7] has disappeared.

When cucurbitacin B in acetic acid was treated with zinc dust for 4 hr. at room temperature, a new product was obtained. The ultraviolet and infrared spectra showed that the α,β-unsaturated carbonyl system had disappeared. Although cucurbitacin B gave only a pale yellow color with tetranitromethane, the new compound gave an orange color, indicating the production of a highly alkylated isolated double bond. Analysis showed that the new

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(1) D. Lavie and Y. Shvo, *Proc. Chem. Soc.*, 220 (1958).

(2) D. Lavie, Y. Shvo, and D. Willner, *Chem. and Ind.*, 1361 (1958).

(3) D. E. A. Rivett and P. R. Enslin, *Proc. Chem. Soc.*, 1958, in press. We wish to thank Dr. Enslin for sending us a copy of this Communication.

(4) Private communication from Dr. P. R. Enslin summarizing a note sent to Chemistry and Industry in December, 1958.

(5) W. O. Eisenhut and C. R. Noller, Abstracts of paper presented at the San Francisco meeting of the American Chemical Society, April 1958.

(6) D. E. A. Rivett and F. H. Herbstein, *Chemistry and Industry*, 393 (1957).

(7) P. R. Enslin, S. Rehm, and D. E. A. Rivett, *J. Sci. Food Agr.*, **8**, 673 (1957).

(8) W. O. Eisenhut and C. R. Noller, *J. Org. Chem.*, **23**, 1984 (1958).