plants[20] and first applied to paper chromatography by Fink, *et al.*[21] This technique was adapted and extensively used by Benson, *et al.*,[9] for the identification of photosynthetic products. Since the salt necessary to maintain the chloroplasts in an active state interfered with the chromatograms, the extracts were further treated by passing them through a column of Amberlite IR-100 (hydrogen form). The column, about 15 cm. long and 2 cm. in diameter, was prepared by gravity sedimentation of an aqueous suspension of the resin.

The sample to be desalted (about $^9/_{10}$ of the soluble fraction) was diluted with water to 50 ml. and passed through the column at a rate of 2–3 ml. per min. The column was then washed with water (150 ml.) at a similar rate of flow, and the combined eluate and washings, representing the "acid plus neutral" fraction, was evaporated to a small volume (0.7 ml.) at 30° under reduced pressure. The "basic" fraction, which was adsorbed on the resin, was eluted with aqueous ammonia (approx. 2 *N*). The elution was continued until ammonia could be detected in the eluate. The eluate of the "basic" fraction was reduced in volume in the same way as the "acid plus neutral" fraction. Aliquots of the desalted fractions were used for paper chromatography. The "acid plus neutral" fraction contained phosphorylated sugars and organic acids and the "basic" fraction contained the amino acids.

Dihydroxyacetone, alanine, glycine, aspartic acid, malic acid and glycolic acid were identified by cutting out spots from the paper and co-chromatographing with authentic samples of these compounds in the phenol water and butanol–acetic acid mixtures. Identity of the unknown with the authentic compound was evidenced by the appearance of a single spot. Additional evidence for the identity of the amino acids was obtained after deaminating a sample of radioactive material, mixed with carrier, by treatment with a mixture of KNO_2 and glacial acetic acid. The resulting hydroxy acids were then identified by co-chromatography on paper.

Sugar phosphates were identified by eluting the radioactive material from the paper, adding to the eluate 0.05 ml. of 0.2 *M* tris-(hydroxymethyl)-aminomethane buffer, *p*H 8.8, and 0.2 ml. of a solution of alkaline phosphatase (General Biochemicals, 4 mg. per 10 ml.), then incubating at 38° for two to three hours. The phosphatase treated material was then co-chromatographed with authentic sugars.

(20) D. I. Arnon, P. R. Stout and F. Sipos, *Amer. J. Bot.*, **27**, 791 (1940).

(21) R. M. Fink, D. E. Dent and K. Fink, *Nature*, **160**, 801 (1947).

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NOTES

Unsaturated Phenols. II.[1] Attempted Syntheses of *o*-Vinylphenol

BY ALFRED R. BADER

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As part of a more extensive study of unsaturated phenols, small quantities of *o*-vinylphenol were required. At least five apparently convenient syntheses are described in the literature: (i) the reaction of phenol with ethylene oxide,[2] (ii) the sulfuric acid-catalyzed rearrangement and dehydration of β-phenoxyethanol,[2] (iii) the reaction of vinyl acetate with phenol,[3] (iv) the decarboxylation of *o*-hydroxycinnamic acid,[4] and (v) the thermal decomposition of the benzodioxin obtained from phenol and acetaldehyde.[5]

Smith and Niederl claimed that phenol and ethylene oxide react in the presence of sulfuric acid to give a 65% yield of *o*-vinylphenol, characterized by its tetrabromide and phenoxyacetic acid reported previously.[4b] Many attempts to repeat the work of Smith and Niederl were unsuccessful. The ultraviolet spectrum of the crude reaction product, mainly unreacted phenol, showed no conjugated unsaturation. The crude reaction product was brominated, and the bromophenols were separated by chromatography; no tetrabromide, easily obtained from *o*-vinylphenol, could be isolated.

Smith and Niederl[2] postulated β-phenoxyethanol as the intermediate in the formation of *o*-vinylphenol from phenol and ethylene oxide. Support for this was found in the alleged reaction of β-phenoxyethanol with sulfuric acid at room temperature to yield *o*-vinylphenol. Actually, β-phenoxyethanol is recovered unchanged from the reaction conditions described (identical infrared spectra and physical constants).[6]

The reaction of vinyl acetate with phenol in the presence of sulfuric acid has been reported[3] to yield a polymer from which *o*-vinylphenol has been alleged to be easily obtainable by thermal depolymerization. The product of the very vigorous reaction is a polymer, but no *o*-vinylphenol could be obtained therefrom.

The decarboxylation of *o*-hydroxycinnamic acid[4] provides a convenient method for the preparation of *o*-vinylphenol.

(1) For paper I see THIS JOURNAL, **75**, 5967 (1953).

(2) R. A. Smith and J. B. Niederl, *ibid.*, **53**, 806 (1931).

(3) J. B. Niederl, R. A. Smith and M. E. McGreal, *ibid.*, **53**, 3390 (1931).

(4) (a) H. Kunz-Krause and P. Manicke, *Arch. Pharm.*, **566**, 555 (1929); (b) K. Fries and G. Fickewirth, *Ber.*, **41**, 367 (1908).

(5) E. Adler, H. v. Euler and G. Gie, *Arkiv Kemi, Mineral., Geol.*, **16A**, No. 12, 1 (1943); *C. A.*, **38**, 5839 (1944).

(6) Adler, *et al.*,[5] also were unable to obtain *o*-vinylphenol from β-phenoxyethanol.

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Steroids. LXVIII.[1] 17-Ethylepitestosterone

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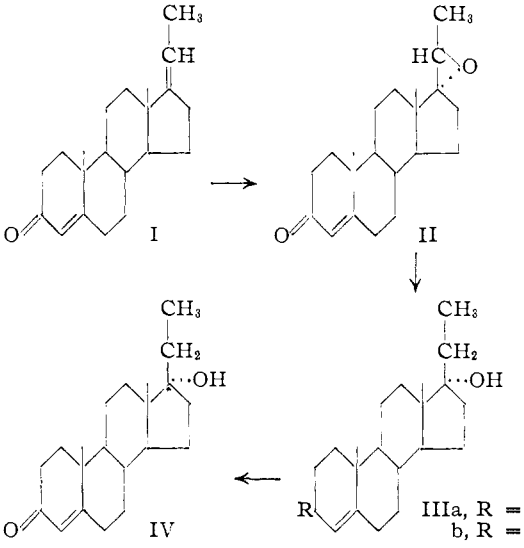
RECEIVED FEBRUARY 14, 1955

In view of the facile preparation of 17-methylepitestosterone from 17-methylene-Δ^4-androsten-3-one through preferential epoxidation of the exocyclic double bond, followed by lithium aluminum hydride reduction and manganese dioxide oxidation,[1] we decided to prepare the hitherto unknown 17-ethylepitestosterone (IV) by an analogous route. This substance was required for testing for possible ana-

(1) Paper LXVII, F. Sondheimer, O. Mancera, M. Urquiza and G. Rosenkranz, THIS JOURNAL, **77**, 4145 (1955).

bolic properties. Moreover the compound is of interest since it contains the 3-keto-17α-hydroxy-Δ^4-pregnene system of which cortisone and hydrocortisone are 11,20,21-oxygenated derivatives.

We employed $\Delta^{4,17(20)}$-pregnadien-3-one (I) as starting material, a substance prepared most readily from 17α-ethinyl-Δ^5-androstene-3β,17β-diol by reduction with sodium in alcohol to $\Delta^{5,17(20)}$-pregnadien-3β-ol, followed by Oppenauer oxidation.[2] The epoxidation of the $\Delta^{17(20)}$-double bond of I previously had been attempted through reaction with monoperphthalic acid (1.5 equivalents).[3] At least three different substances were produced (none isolated in the pure state in more than a few per cent. yield) to which no definite structural assignments were given. We oxidized I with 0.9 of an equivalent of perbenzoic acid, since these conditions had yielded the most favorable results with the corresponding 17-methylene compound.[1] The product, isolated in 61% yield, was the required 17α,20-oxide II as evidenced by the elementary analysis, infrared and ultraviolet spectrum, its subsequent transformation to IV and by the now well-established predominant α-attack at C-17.[4] The oxide II corresponds in physical properties most closely to the isomer B of Ruzicka, *et al.*[3]



Treatment of II with lithium aluminum hydride under the usual conditions (refluxing in ether or tetrahydrofuran) only served to reduce the Δ^4-3-ketone function, since oxidation of the product yielded the initial oxide II. Only by carrying out the lithium aluminum hydride reduction in refluxing dioxane for an extended period could the oxide ring be cleaved, for manganese dioxide oxidation then furnished a substance (72% yield) which differed from II and which showed infrared bands corresponding both to an α,β-unsaturated ketone and to a hydroxyl group. Confirmation for the 17-ethylepitestosterone structure IV with its tertiary hydroxyl group was obtained for this compound by the fact that it was recovered unchanged on attempted acetylation; the other possible reduction product would have possessed the secondary 20-hydroxyl function. Thus, lithium aluminum hydride reduction of the oxide again has yielded the axial hydroxyl group.

The 17-ethylepitestosterone (IV) differed from the known 17-ethyltestosterone, which might in principle have been formed had the oxide II possessed the 17β-structure. The structure of IV was further confirmed by its molecular rotation (+256) which is nearly identical with that of 17-methylepitestosterone (+248)[1] and also with those of 17-ethyltestosterone (+254)[5] and 17-methyltestosterone (+245).[6]

Experimental[7]

17α,20-Oxido-Δ^4-pregnen-3-one (II).—A solution of 2 g. of $\Delta^{4,17(20)}$-pregnadien-3-one (I) (m.p. 136–138°)[2] in 10 cc. of chloroform was oxidized by the portionwise addition of 16 cc. of a chloroform solution containing 0.9 equivalent of perbenzoic acid. The reaction was exothermic and the temperature of the solution was kept at 15–20° during the addition by ice-cooling. After being allowed to stand at room temperature overnight, the solution was diluted with chloroform and washed with water and sodium carbonate solution. Drying, evaporation and crystallization of the solid residue from ether–hexane furnished 1.28 g. (61%) of the oxide II with m.p. 179–184° (Kofler). A further purified sample showed m.p. 184–185° (Kofler), $[\alpha]_D$ +110°, $\lambda_{max.}$ 240 mμ, log ϵ 4.23, $\nu_{max.}$ 1660 cm.$^{-1}$; reported by Ruzicka, *et al.*,[3] for isomer B: m.p. 188.5–190°, $[\alpha]_D$ +106°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 79.98; H, 9.67.

Δ^4-Pregnen-17α-ol-3-one (17-Ethylepitestosterone) (IV).—The oxide II (0.7 g.) in 90 cc. of dioxane (previously distilled over sodium) was added gradually to a solution of 1 g. of lithium aluminum hydride in 50 cc. of dry ether. The mixture was distilled until most of the ether had been removed and was then refluxed for 8 hours. Ethyl acetate was added to decompose the excess reagent and the product was isolated by the sodium sulfate procedure, as described previously.[1] The solid residue, consisting of IIIa and IIIb, showed no high intensity absorption in the ultraviolet and was not purified. It was dissolved in 60 cc. of chloroform and shaken with 3.5 g. of manganese dioxide (reference 1, footnote 17) for 16 hours. Since the ultraviolet spectrum of an aliquot showed oxidation not to be quite complete, another 3.5 g. of dioxide was added and shaking was continued for a further 16 hours. The solid was removed and washed well with hot chloroform. Evaporation of solvent and crystallization of the residue from acetone–hexane produced 0.51 g. (72%) of 17-ethylepitestosterone with m.p. 145–148°. Further purification produced the analytical specimen with m.p. 152–153° (Kofler), $[\alpha]_D$ +81°, $\lambda_{max.}$ 240 mμ, log ϵ 4.22, $\nu_{max.}$ 1660 cm.$^{-1}$ and free hydroxyl band. On admixture with a sample of 17-ethyltestosterone (m.p. 138–140°, $[\alpha]_D$ +82°) a m.p. depression of *ca.* 30° was observed. On attempted acetylation (pyridine–acetic anhydride, 24 hours, 20°) IV was recovered unchanged.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.39; H, 10.14.

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(2) L. Ruzicka, M. W. Goldberg and E. Hardegger, *Helv. Chim. Acta*, **22**, 1294 (1939); see also A. Butenandt, J. Schmidt-Thomé and H. Paul, *Ber.*, **71**, 1313 (1938), for preparation of I by dehydration of 17α-ethyltestosterone.

(3) L. Ruzicka, M. W. Goldberg and E. Hardegger, *Helv. Chim. Acta*, **25**, 1297 (1942).

(4) L. F. Fieser, *Experientia*, **6**, 312 (1950).

(5) E. B. Hershberg, E. P. Oliveto, C. Gerold and L. Johnson, THIS JOURNAL, **73**, 5073 (1951).

(6) Determined in these laboratories. All rotations in chloroform.

(7) Rotations were measured at 20° in chloroform and ultraviolet absorption spectra in 95% ethanol solution. Infrared spectra were determined in chloroform solution on a Perkin-Elmer model 12 C single beam spectrophotometer with sodium chloride prism. Thanks are due to Mrs. P. López and staff for the aforementioned measurements and to Mrs. A. González for the microanalyses.