microns, and a strong band at 5.78 microns was present in the spectrum of the ketone.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.5; H, 9.8. Found: C, 80.8; H, 9.7.

The colorless semicarbazone was prepared[10] and recrystallized from 25% ethanol, m.p. 188–189°.

Anal. Calcd. for $C_{12}H_{19}ON_3$: C, 65.2; H, 8.6. Found: C, 65.2; H, 8.6.

The 2,4-dinitrophenylhydrazone derivative formed as orange flakes, m.p. 144–145° (from 95% ethanol).

Anal. Calcd. for $C_{17}H_{20}O_4N_4$: C, 59.3; H, 5.8; N, 16.3. Found: C, 59.6; H, 6.0; N, 16.6.

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The Diels-Alder Reaction of Steroidal 20-Methylene-Δ^{16}-pregnene Derivatives with Maleic Anhydride

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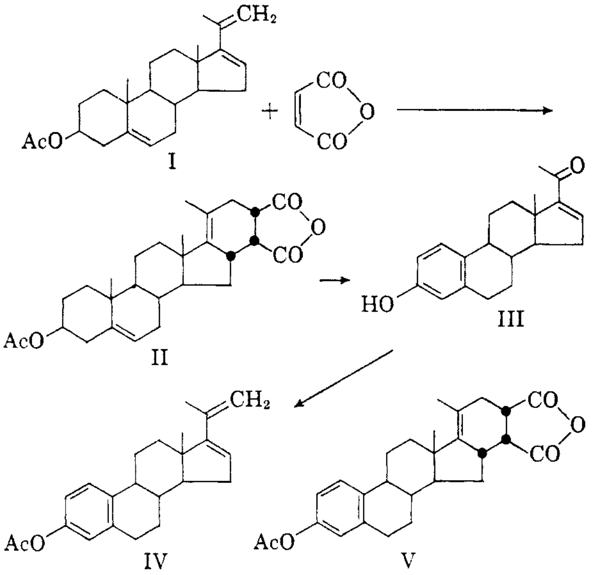
We have recently described[1] the synthesis of 20-methylene-$\Delta^{5,16}$-pregnadien-3β-ol acetate (I) by treatment of the corresponding 20-ketone with triphenylphosphine-methylene. The novel $\Delta^{16,20(22)}$-diene system present in I should permit its condensation with dienophiles in a Diels-Alder type of reaction to produce substances containing an additional ring (or rings) fused to the 16 and 17 positions of the steroid nucleus. Indeed when the triene I was allowed to react with maleic anhydride in boiling benzene, an adduct was obtained stereospecifically in excellent yield, which on the basis of the elemental analysis and spectral properties must be the pentacarbocyclic compound II. The β-configuration of the hydrogen substituent at C-16 is based on the expectation that attack of the dienophile proceeds from the less hindered α-side of I.[2] The β-hydrogen configuration at the other two new asymmetric centers follows from the rule of maximum accumulation of unsaturation in the transition state of the complex formed in the Diels-Alder reaction.[3]

In the 19-nor steroid series, 17-acetyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol (III)[4] on treatment with triphenylphosphinemethylene and subsequent acetylation yielded the 19-nor-20-methylene-Δ^{16}-derivative IV, which was smoothly converted to the adduct V by means of maleic anhydride in boiling benzene. The Diels-Alder reaction between 20-methylene-Δ^{16}-pregnenes and maleic anhydride therefore appears to be general.[5]



EXPERIMENTAL[6]

Adduct II from 20-methylene-$\Delta^{5,16}$-pregnadien-3β-ol acetate (I) *and maleic anhydride.* A solution containing 100 mg. of the triene I (m.p. 124.5–126°)[1] and 100 mg. of freshly sublimed maleic anhydride in 10 cc. of dry benzene was boiled under reflux for 6 hr., cooled, and diluted with water. The organic layer was washed with 2% sodium hydroxide solution and water and was then dried and evaporated. The solid residue (108 mg.) showed m.p. 235–245° and after one crystallization from ether gave the analytical sample of the adduct II as needles with constant m.p. 255–256°, $[\alpha]_D$ −26°, ν_{max} 1860, 1780 cm.$^{-1}$ (5-membered cyclic anhydride) and 1735 cm.$^{-1}$ (acetate), no high-intensity absorption in the ultraviolet.

Anal. Calcd. for $C_{28}H_{36}O_5$: C, 74.30; H, 8.02. Found: C, 74.23; H, 7.88.

17-Isopropenyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol acetate (IV) *from 17-acetyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol* (III). A 1*N* ethereal solution of butyllithium (10 cc.) was added to a suspension of 3.57 g. (10 millimoles) of methyltriphenylphosphonium bromide in 50 cc. of ether with swirling under nitrogen. The mixture was shaken in nitrogen for 2 hr., and a solution of 590 mg. (2 millimoles) of 17-acetyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol (III)[4] in 30 cc. of dry ether was then added. The mixture was shaken for a further 4 hr. and allowed to stand overnight at room temperature. Tetrahydrofuran was then added at the same time as the ether was distilled off until most of the latter had been replaced. The mixture was boiled

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[1] F. Sondheimer and R. Mechoulam, *J. Am. Chem. Soc.*, **79**, 5029 (1957).

[2] *Cf.* L. F. Fieser, *Experientia*, **6**, 312 (1950).

[3] *Cf.* K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937).

[4] C. Djerassi, G. Rosenkranz, I. Iriarte, J. Berlin, and J. Romo, *J. Am. Chem. Soc.*, **73**, 1523 (1951).

(5) Since our work was completed, two patents have appeared describing the Diels-Alder reaction between 20-acetoxy-$\Delta^{16,20}$-pregnadiene derivatives and maleic anhydride [R. H. Mazur and G. P. Mueller, U. S. Patent **2,753,343**, July 3, 1956; *Chem. Abstr.*, **51**, 2070 (1957); R. H. Mazur, U. S. Patent **2,753,359**, July 3, 1956; *Chem. Abstr.*, **51**, 4436 (1957)].

(6) Melting points are uncorrected. Rotations were determined at 20–25° in chloroform solution. Ultraviolet spectra were measured on a Unicam Model S.P. 500 spectrophotometer and infrared spectra (in chloroform solution) on a Baird double beam recording spectrophotometer with sodium chloride prism. Analyses were carried out in our microanalytical laboratory under the direction of Mr. Erich Meier.

under reflux for 6 hr., cooled, and diluted with ether and water. The organic layer was washed with water, dried and evaporated to dryness. The residue was acetylated by being allowed to stand overnight at room temperature with 10 cc. of pyridine and 10 cc. of acetic anhydride. The product was isolated with ether in the usual way and chromatographed on 25 g. of Merck "acid-washed" alumina. The fractions eluted with petroleum ether-benzene (4:1) on crystallization from methanol yielded 290 mg. of the pentaene acetate IV with m.p. 118–120°. The analytical sample showed m.p. 132–133°, $[\alpha]_D + 65°$, ν_{max} 1750 (phenyl acetate), 1620 and 890 cm.$^{-1}$ (terminal methylene), λ_{max} 239 mμ (log ϵ 4.22) (iso-octane).

Anal. Calcd. for $C_{23}H_{28}O_2$: C, 82.10; H, 8.39. Found: C, 82.11; H, 8.39.

Adduct V from 17-isopropenyl-$\Delta^{1,3,5(10),16}$*-estratetraen-3-ol acetate* (IV) *and maleic anhydride.* A solution of 60 mg. of the pentaene acetate IV and 60 mg. of maleic anhydride in 6 cc. of benzene was boiled under reflux for 6 hr. Isolation as previously and crystallization from ether gave 35 mg. of the adduct V with m.p. 178–182°. Further crystallization from ether gave the analytical specimen with m.p. 182–184°, $[\alpha]_D +83°$, ν_{max} 1850, 1780 cm.$^{-1}$ (5-membered cyclic anhydride) and 1760 cm.$^{-1}$ (phenyl acetate), λ_{max} 268 mμ (log ϵ 2.98) (95% ethanol).

Anal. Calcd. for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.44; H, 7.02.

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Improved Yields in the Preparation of Diacetyl Peroxide

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In connection with some studies on the oxidation of cyclohexene[1] and on the stability of acyloxy radicals it was necessary to prepare reasonably large amounts of pure diacetyl peroxide in the solid state. The several methods of preparation available in the literature were found unsuitable. Thus, Shanley's method[2] is suitable for small amounts only, Walker's method[3] appeared too dangerous for large scale use, particularly in warm climates, and a patented method[4] involved an unsuitable solvent. The well-known method of Gambarjan,[5] outlined by Shirley[6] gave variable and poor yields. However, by modifying Gambarjan's method it was possible to prepare diacetyl peroxide in 79% yield, and the peroxide obtained was of excellent purity. Although Kuhn[7] recommends using the peroxide within 24 hours when it is prepared by Gambarjan's method, we were able to store the peroxide in Dry Ice and use it a week later. However, we do not recommend this as a general practice. Where it is necessary to prepare the solid peroxide for subsequent investigation in a particular solvent we recommend adding the solvent to the peroxide before removing the peroxide container from its Dry Ice surroundings.

EXPERIMENTAL

A solution of 87 g. (0.723 mole) acetic anhydride in 450 ml. of ether, freshly distilled after standing over sodium, was placed in a 1 liter Erlenmeyer flask in an ice bath. To the flask was added 43.5 g. (0.558 mole) of sodium peroxide in one portion. The mixture was stirred mechanically and distilled water (150 ml.) was added to it dropwise until all of the sodium peroxide had dissolved. The addition of the water took approximately 10 hr. and was controlled so as to keep the temperature of the mixture below 5° and to avoid, as much as possible, the evolution of oxygen. After the addition was finished the ether layer was separated and the aqueous layer was extracted with two 100-ml. portions of ether. The combined ether solutions were washed with two 100-ml. portions of 1% sodium bicarbonate solution to remove acetic acid. The ether solution was then dried over calcium chloride for 2 hr., carefully decanted into a tared, standard taper flask, which was equipped with a calcium chloride tube, and allowed to stand in a Dry Ice–alcohol slurry overnight. A large crop of solid peroxide crystals formed. This was not removed. Instead, the flask was raised slightly above the rim of the Dewar vessel, and the ether was removed at low pressure.

Iodimetric assay[8] gave a peroxide content of 98.97%. Small amounts of the solid peroxide were removed from the flask with a porcelain spatula for assay and quickly transferred to a weighing bottle containing a known weight of isopropyl alcohol. Large amounts of solid peroxide were *never* removed from the flask; instead the peroxide was dissolved in the required solvent and used in a manner to be described in a later publication.

Although this procedure takes longer than Gambarjan's[5] it has been found to be much more reliable and consistent in its results. For example, two representative runs using the quantities above gave 39.6 g. (79% yield) and 39.2 g. (77.8% yield), the yields being based on acetic anhydride. In contrast, by following Gambarjan's procedure, as described by Shirley,[6] yields varying from 9.1 to 43.3% were obtained in 5 attempts.

No trouble was experienced at any time during preparations as outlined above. During the removal of the ether by pumping and during storage and handling of the flask containing the solid peroxide the apparatus was shielded by safety screens. The solid was never allowed to approach its melting point and was never brought into contact with anything but glass or porcelain surfaces. Whenever possible the apparatus containing the solid peroxide was handled with tongs.

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