treated with acetone and sulfuric acid a second time. The combined isopropylidene derivatives (0.86 g., 41%) were heated under reflux with 50% acetic acid (14 ml.) for 2 hr. and the resulting yellow oily solid (0.66 g.) was treated with *p*-nitrobenzoyl chloride (1.5 g.) in anhydrous pyridine (10 ml.) for 2 days: (+)-camphane-2-*endo*,3-*endo*-diol di-*p*-nitrobenzoate, m.p. 169.5–170.5°, $[\alpha]_D$ +28.5° (*c* 0.4 in $CHCl_3$), was obtained.

The dark residue (0.67 g.) from the distillation of the isopropylidene derivative was sublimed at 120° (1 mm.) to give a colorless, crystalline solid (0.53 g.), $[\alpha]_D$ +8° (*c* 1. 4in EtOH). Esterification gave a crude di-*p*-nitrobenzoate (1.37 g., 93%), $[\alpha]_D$ +69° (*c* 1.3 in $CHCl_3$) from which—by crystallization from ethanol—the quasi-racemic di-*p*-nitrobenzoate (0.9 g.), m.p. 152–154°, and (+)-camphane-2-*exo*,3-*endo*-diol di-*p*-nitrobenzoate, m.p. 123–125°, were isolated.

The Camphane-2,3-diol Diacetates.—Each diol (2.2 g.) was heated with acetic anhydride (20 ml.) and anhydrous sodium acetate (1 g.) for 6 hr. on a steam-bath. After cooling, the solution was diluted with water, extracted with ether, the solvent dried (Na_2SO_4) and evaporated, and the residue distilled to give the diacetate as a colorless oil. Crude yields, b.p.'s, $[\alpha]_D$ values in ethanol, and analyses were: (−)-2-*exo*,3-*exo*: 79%, 140–145° (5.5 mm.), −10° (*c* 3); C, 66.15; H, 8.65; (+)-2-*endo*,3-*endo*: 86%, 98° (0.5 mm.), +39° (*c* 4); C, 66.3; H, 8.85; (+)-2-*endo*,3-*exo*: 96%, 89–90° (0.4 mm.), +26° (*c* 4); C, 66.35; H, 9.0; (+)-2-*exo*,3-*endo*: 75%, 94° (0.6 mm.), 0° (*c* 2); C, 66.35; H, 8.8. Calcd. for $C_{14}H_{22}O_4$: C, 66.1; H, 8.7.

Comparative Rates of Hydrolysis of the Camphane-2,3-diol Diacetates.—Solutions (0.025 *M*) of the diacetates were used. The required amount of the diacetate was weighed into a 100-ml. volumetric flask, dissolved in 75% ethanol (v./v.) and immersed, together with a *N* solution of sodium hydroxide, in a constant temperature bath at 22.5° (±0.3) (except for the 2-*exo*,3-*endo*-isomer which was treated at 25°). After 0.5 hr., 5 ml. of the sodium hydroxide solution was added to the solution of the diacetate and the mixture diluted to the mark. At time intervals 10-ml. aliquots were removed, cooled in a Dry Ice–ethanol mixture and titrated with standard hydrochloric acid. The results are shown in Fig. 1.

Hydrogen Bonds.—Infrared spectra were taken and evaluated according to Kuhn's method.[24] The carbon tetrachloride used as the solvent was distilled over P_2O_5 and stored over P_2O_5. The measurements were made with a Perkin–Elmer double-beam recording spectrophotometer equipped with a quartz prism, on solutions less than 0.005 *M* in 2- and 4-cm. cells. Hydroxy bands were found at the following frequencies: 2-*exo*,3-*exo*: 3641 and 3545 cm.$^{-1}$, 2-*endo*,3-*endo*: 3635 and 3540 cm.$^{-1}$, 2-*exo*,3-*endo*: 3631 cm.$^{-1}$ and 2-*endo*,3-*exo*: 3628 cm.$^{-1}$.

Kinetic Runs. (a) **Lead Tetraacetate and Phenyl Iodosoacetate.**—Acetic acid was successively treated with chromic oxide and boron triacetate.[33] Runs with the *cis*-glycols were carried out in "Dreischenkelrohr"[34] tubes using Criegee's fast method. Solutions (5 ml. of each) of the diols (0.0005 − 0.001 *M*) and the oxidizing agent (0.0125 − 0.02 *M*) in glacial acetic acid were placed in each of the lower bulbs of the "Dreischenkelrohr." Ten ml. of "stopping solution" (50 g. of potassium iodide and 250 g. of sodium acetate in 1 l. of water) was placed in the side bulb. After 15 min. in the thermostat, the reaction solutions were mixed and, at a definite time, the "stopping solution" was added. The liberated iodine was titrated with 0.02 *N* thiosulfate solution.

The *trans*-glycols (*ca.* 1.5 × 10^{-4} mole) were weighed into a 50-ml. volumetric flask and, after thermostating, were dissolved in the solution of the oxidizing agent (0.0125–0.02 *M*). At intervals, 5-ml. aliquots were added to 10 ml. of stopping solution and titrated as above. Blank titrations were always run.

(b) **Periodate.**—The following buffer solutions were used: (i) *p*H 10.45: 0.1 *N* hydrochloric acid (100 ml.) and sodium carbonate (5.301 g.) in 1 l. of water; (ii) *p*H 2.12: *N* sodium acetate (200 ml.) and *N* hydrochloric acid (200 ml.) diluted with water to 1 l. The ionic strength was maintained constant by dissolving sufficient sodium nitrate in each buffer to make it 0.2 *M*. Solutions of sodium metaperiodate (0.001 *M*), which were also 0.2 *M* in sodium nitrate, were made up in the same buffers. The glycols were dissolved in ethanol (1 vol.) and the solution diluted with buffer (9 vols.).

Runs with the *cis*-diols (*p*H 10.45) were made in the "Dreischenkelrohr" as described above. The "stopping solution" was *M* in potassium iodide and *M* in sodium hydrogen carbonate; 0.0016 *N* arsenite solution was used for the titrations. The initial concentration of the glycols was 0.00128 *M* and that of periodate, 0.000585 *M*.

Solutions of the *trans*-glycols (*p*H 2.12) were made up to 50 ml. and, at intervals, 5-ml. aliquots were removed. The "stopping solution" (10 ml.) was 0.1 *N* hydrochloric acid containing a few crystals of potassium iodide. The liberated iodine was titrated with 0.007 *N* thiosulfate solution. The initial glycol concentration was 0.00123 *M* and that of periodate, 0.00077 *M*.

The rate constants were calculated as described by Cordner and Pausacker.[35]

(33) W. C. Eichelberger and V. K. LaMer, THIS JOURNAL, **55**, 3633 (1933).

(34) R. Criegee, *Ann.*, **495**, 211 (1932).

(35) J. P. Cordner and K. H. Pausacker, *J. Chem. Soc.*, 102 (1953).

SYDNEY, AUSTRALIA

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

Reaction of Diazomethane with Δ^{16}-20-Keto Steroids[1]

BY H. L. SLATES AND N. L. WENDLER

RECEIVED APRIL 2, 1959

The reaction of 3α-acetoxy-Δ^{11}-pregnene-11,20-dione with diazomethane and the products formed consequent to pyrolysis of the intermediate pyrazoline derivative are discussed.

The reaction of diazomethane with Δ^{16}-20-keto steroids was first studied by Wettstein[2] who prepared the pyrazoline derivatives corresponding to 16-dehydropregnenolone, its acetate and 16-dehydroprogesterone. The major product formed from the pyrolysis of these derivatives was formulated by Wettstein as a 16-methyl-16-dehydro-20-keto system and this structure has received unequivocal confirmation recently from the work of Romo, Lepe and Romero.[3] In this connection, these authors demonstrated the identity of the major compound from the pyrazoline pyrolysis with the product obtained from kryptogenin on treatment with methyl Grignard with subsequent side chain degradation. They found further that the same compound was obtained by bromination and dehydrobromination of the 16-methyl-20-ketone produced from the corresponding 16-dehydro-20-ketone with methyl Grignard. Wettstein also

(1) Presented at the Meeting-in-Miniature of the North Jersey Section of the American Chemical Society on January 26, 1959.

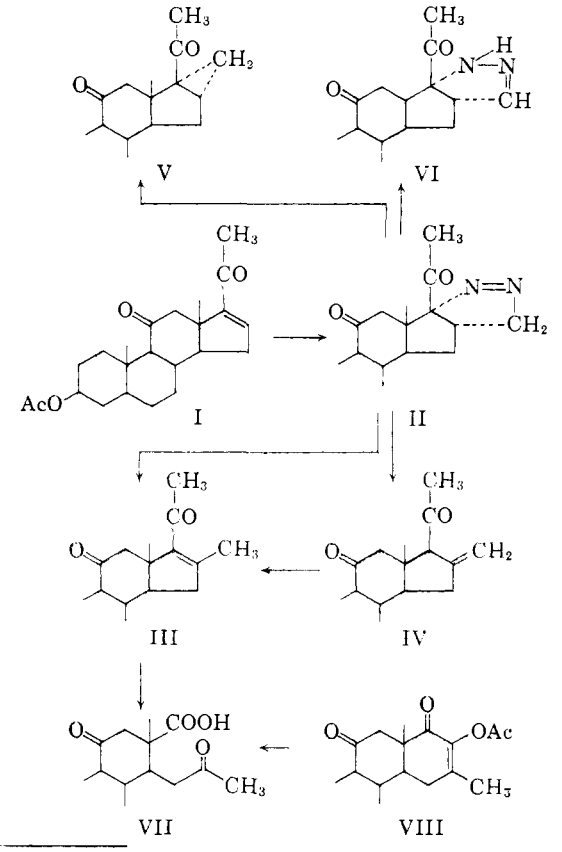
(2) A. Wettstein, *Helv. Chim. Acta*, **27**, 1803 (1944).

(3) J. Romo, J. Lepe and M. Romero, *Bol. Inst. Quim. Univ. Auton. Mex.*, **4**, 125 (1952).

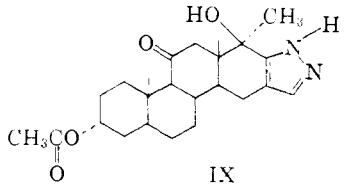
isolated a minor by-product from the pyrolysis reaction which he correctly formulated as the cyclopropyl ketone (16,17-methylene-20-ketone). The structure of the latter substance has since been confirmed by spectral information provided by Sandoval, Rosenkranz and Djerassi.[4]

In a similar vein Mueller and Riegel[5] allowed diazoacetic ester to react with 16-dehydropregnenolone and obtained the corresponding Δ^2-pyrazoline derivative in contrast to the Δ^1-structure experienced with diazomethane. These workers found further that whereas the free pyrazoline carboxylic acid on pyrolysis gave 16-methyl-16-dehydro-20-ketone, the ester itself gave largely a mixture of isomeric cyclopropyl derivatives. They interpreted the fate of the free acid as initially undergoing decarboxylation to the diazomethane adduct.

Recently we had occasion to prepare 16-methylated cortical steroids[6] and to this end we availed ourselves of the reaction of diazomethane with 3α-acetoxy-Δ^{16}-pregnene-11,20-dione (I). Formation of the pyrazoline II proceeded smoothly in ether solution and in high yield. Pyrolysis of the pyrazoline II,[7] by adapting the method of Wettstein[3] to our series, was found to produce a three-component product system. The latter consisted not only



of the 16-methyl-Δ^{16}-20-ketone III as the major product together with small amounts of the cyclopropyl ketone V, but also contained the exomethylene ketone IV as demonstrated by the latter's spectra and subsequent transformations. The exomethylene ketone represents a long missing third possible product from a diradical recombination visualized as arising from the pyrolysis reaction. The Δ^1-pyrazoline derivative II on treatment with base was isomerized to the Δ^2-pyrazoline system VI. The isomerization of II $\rightarrow$ VI was accompanied by a shift of the 6.4μ band in the infrared associated with the —N=N— grouping to 6.2 μ (>C=N)– as well as the appearance of an >N—H function ascertained by formation of an amide derivative on formylation and acetylation. Similar alkaline isomerization of the Δ^1-pyrazoline derived from 3β-hydroxy-$\Delta^{5,16}$-pregnadiene-20-one produced a Δ^2-pyrazoline similar to VI and exhibiting strong carbonyl absorption in the infrared. The latter observation excludes the possibility of D-homoannulation during the alkaline isomerization to a system with the structure IX.[8]



The $\Delta^{\alpha,\beta}$-unsaturated ketone III, the major product from the pyrolysis of the Δ^1-pyrazoline II, was formed in 85% yield with a m.p. 165–167° and $\lambda_{max}^{CH_3OH}$ 248 mμ (9,300). Oxidation of III with potassium permanganate produced the ketonic acid VII which was identical by infrared comparison with a sample prepared by similar oxidation of the diosphenol derivative VIII.[9]

The mother liquors after separation of the 16-methyl-Δ^{16}-20-ketone III were chromatographed on neutral alumina. Material eluted with benzene corresponded to the cyclopropyl ketone V with m.p. 171–173°, $E_{220\ mu}$ 5,800 and $\lambda\lambda_{max}^{chf}$ 5.78 (OAc), 5.83 (11 C=O) and 5.93 μ (20 C=O conj. with cyclopropane). The ultraviolet spectrum as well as the conjugated 20 C=O band at 5.93 μ in the infrared corresponds to those ascertained in another series[4] for this system.

(4) A. Sandoval, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 2383 (1951).

(5) G. P. Mueller and B. Riegel, *ibid.*, **76**, 3086 (1954).

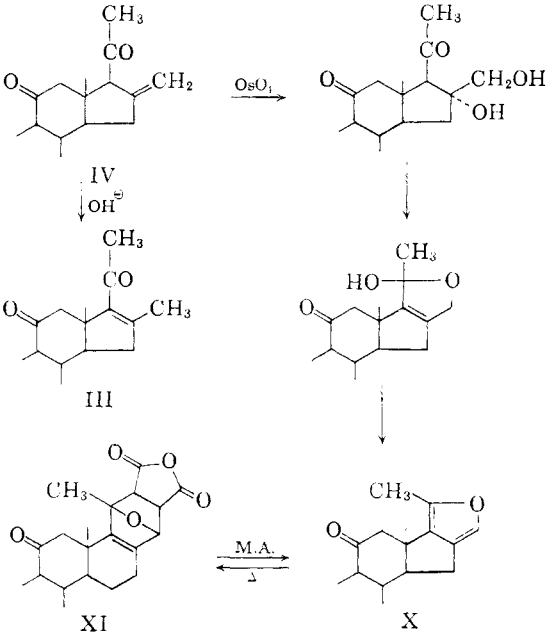
(6) D. Taub, R. D. Hoffsommer, H. L. Slates and N. L. Wendler, *ibid.*, **80**, 4435 (1958); see also E. P. Oliveto, R. Rausser, A. L. Nussbaum, W. Gebert, E. B. Hershberg, S. Tolksdorf, M. Eisler, P. L. Perlman and M. M. Pechet, *ibid.*, **80**, 4428 (1958).

(7) The α-orientation of the pyrazoline ring fusion follows from the generalized rule of the rear-attack experienced with Δ^{11}-20-keto systems.

(8) The D-homo system IX was originally believed to represent the structure of the alkaline isomerization product of II wherein the 3-Ac is retained in the isomerization. This followed from the observation that the latter, after acetylation, exhibited both H-stretch as well as amide ($CH_3CON<$) absorption. The nuclear magnetic resonance spectrum of the acetylated product did not, however, corroborate the presence of OH. Further, the n.m.r. spectrum of the alkaline isomerization product itself (which retains the 3-Ac group) indicated only two $CH_3C<$ methyl groups, whereas structure IX requires three. Likewise, two $CH_3C=$ methyl groups were indicated in this product, whereas IX has only one such grouping. These findings supported structure VI wherein the second $CH_3C=$ methyl is provided by the C-17 side chain. In order to corroborate this assignment, alkaline isomerization of the pyrazoline derivative of the 11-desoxo analog 3β-hydroxy-5,16-pregnadiene-20-one was examined, whereby the presence of C=O (C-17 side chain) in the infrared of the isomerization product provided independent substantiation for VI and corresponding rejection of IX.

(9) N. L. Wendler and D. Taub, *Chemistry & Industry*, 415 (1958).

Eluates from the column chromatography corresponding to 20% benzene–petroleum ether afforded the crude exomethylene ketone XIII in an amorphous state exhibiting no ultraviolet maximum but showing the characteristic bands in the infrared for an exomethylene group at 6.05 and 11.2 μ. Treatment of the exomethylene ketone IV with methanolic potassium hydroxide caused quantitative isomerization to crystalline 16-methyl-Δ^{16}-20-ketone III. Hydroxylation of the exomethylene ketone with osmium tetroxide was found to evoke an interesting sequence of changes



The furanoid derivative X was the isolated end-product of the sequence It exhibited characteristic ultraviolet absorption with $E_{222m\mu}$ 6000,[10] and its n.m.r. spectrum demonstrated characteristic furanoid C–H.[11] This compound was allowed to react with maleic anhydride in benzene solution whereupon the adduct XI was formed. The latter could be reversibly converted to the furan on sublimation.

Acknowledgment.—The authors are indebted to R. W. Walker for the determination of infrared spectra and to B. Arison and N. Trenner for determination and interpretation of the n.m.r. spectra.

Experimental[12]

Pyrazoline of 3α-Acetoxypregnane-11,20-dione (II).—To a cold solution of 20 g. of 3α-acetoxy-16-pregnene-11,20-dione in 340 ml. of dry tetrahydrofuran was added an excess of diazomethane in ether solution and the reaction mixture was then allowed to stand at *ca.* 15° overnight. After concentration *in vacuo* and crystallization from acetone–ether there was obtained 14.25 g. of the pyrazoline derivative II, m.p. 186–190° dec.

Anal. Calcd. for $C_{24}H_{34}O_4N_2$: C, 69.55; H, 8.27. Found: C, 69.37; H, 8.01.

Second and third crops of pyrazoline amounting to 6 g., m.p. 180–190°, afforded a total of over 20 g. (90%) of utilizable pyrazoline for the pyrolysis step.

3α-Acetoxy-16-methyl-16-pregnene-11,20-dione (III).—Pyrazoline II (37.4 g.) was placed in a 500-ml. round-bottom flask and heated by an oil-bath *in vacuo* (pressure 0.6 mm.). A manometer and 12-l. surge flask were in the line between the reaction flask and pump trap. When the bath temperature reached 180° the pyrazoline began to melt with evolution of nitrogen. The maximum pressure reached was 83 mm. After 10 minutes at 180–182° the melt was cooled. The pyrolysis residue exhibited at $\lambda_{max}^{CH_3OH}$ 249, $E_{1cm}^{1\%}$ 191, was taken in ~150 ml. of acetone, filtered through Celite, concentrated to ~100 ml. and ether slowly added to the boiling solution until crystallization occurred; yield 19.0 g., m.p. 165–168°; $\lambda_{max}^{CH_3OH}$ 249, $E_{1cm}^{1\%}$ 234; 5.3 g., m.p. 160–164°, $\lambda_{max}^{CH_3OH}$ 249, $E_{1cm}^{1\%}$ 211; 5.0 g., m.p. 142–153°, $\lambda_{max}^{CH_3OH}$ 249, $E_{1cm}^{1\%}$ 156. Total yield of material with $E_{1cm}^{1\%}$ <210 – 70%. The analytical sample melted at 165–167°, $\lambda_{max}^{CH_3OH}$ 248, ϵ 9,300; $\lambda\lambda_{max}^{CHCl_3}$ 5.83, 5.90, 6.05 and 6.23 μ.

Anal. Calcd. for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87. Found: C, 74.30; H, 8.60.

The mother liquors contained additional III as well as the corresponding isomeric cyclopropane and exocyclic olefin. The latter was transformed to III (3α-OM) by methanolic KOH. In a preliminary experiment pyrolysis of the pyrazoline product followed by treatment of methanolic KOH increased the over-all yield of III (3α-ol) from I to about 75%, m.p. 225–228°, $\lambda_{max}^{CH_3OH}$ 248 mμ, ϵ 9,300.

Anal. Calcd. for $C_{22}H_{32}O_3$: C, 76.68; H, 9.34. Found: C, 76.80; H, 9.21.

Isomerization of the Pyrazoline II.—A solution of 3.0 g. of the pyrazoline II in 50 ml. of tetrahydrofuran was treated with 6.0 g. of potassium hydroxide in a minimum volume of water and stirred at room temperature overnight. After concentration *in vacuo* the reaction mixture was extracted with ethyl acetate. The extracts were washed neutral with dilute acid, dried over magnesium sulfate and concentrated *in vacuo* to a foam which readily crystallized from ether to afford the pyrazoline VI, m.p. 157–162°; $\lambda\lambda_{max}^{CHCl_3}$ 2.96, 5.79(sh), 5.85, 6.2 and 7.99μ.

Anal. Calcd. for $C_{24}H_{34}O_4N_2$: C, 69.55; H, 8.27. Found: C, 69.20; H, 8.12.

The nuclear magnetic resonance spectra[13] exhibited resonances at τ = 7.65 ($CH_3\overset{|}{C}=O$) and 7.85 ($CH_3\overset{\|}{C}O-$).

The isomerization product, above, 100 mg., was formylated in 2 ml. of formic acid at 100° for 2 hours. The reaction mixture was diluted with water and the product extracted with ethyl acetate. The ethyl acetate solution was washed with aqueous 5% sodium bicarbonate, water and dried over magnesium sulfate. Removal of the solvent *in vacuo* followed by crystallization from acetone–ether afforded the N-formyl derivative, m.p. 279–281°; λ_{max}^{MeOH} 226, ϵ 8,400; $\lambda\lambda_{max}^{CHCl_3}$ 5.77, 5.84, 5.90 and 61.3 μ.

Anal. Calcd. for $C_{25}H_{34}O_5N_2$: C, 67.84; H, 7.75. Found: C, 67.62; H, 7.68.

Isomerization of the Pyrazoline Derived from 3β-Acetoxy-5,16-pregnadiene-20-one.—A solution of the pyrazoline,[2] 100 mg., in 6 ml. of 5% potassium hydroxide in 5:1 methanol–tetrahydrofuran was refluxed for 2.5 hours. After concentration *in vacuo* and addition of water, the solid product was isolated by filtration. Two crystallizations from ethyl acetate afforded the isomerization product of the alcohol, m.p. 221–228° dec.; $\lambda\lambda_{max}^{solid}$ 2.84, 3.04, 5.93 and 6.21 μ; λ_{max}^{pyr} 5.84 μ.

Anal. Calcd. for $C_{22}H_{32}O_2N_2$: C, 74.13; H, 9.04; N, 7.86. Found: C, 73.89; H, 8.83; N, 7.80.

Isolation of 3α-Acetoxy-16-methylene-pregnane-11,20-dione (IV).—A sample of the residual material from the crystallization of the 16-methyl-Δ^{16}-ketone III, 500 mg., was chromatographed on 25 g. of neutral alumina. The fractions corresponding to 20% benzene in petroleum ether were combined and concentrated to afford *ca.* 150 mg. of a non-crystalline product IV exhibiting no absorption in the ultra-

(10) Compare $E_{222m\mu}$ 5600 for cafestol: C. Djerassi, E. Wilford, L. Viseo and A. J. Lemin, *J. Org. Chem.*, **18**, 1449 (1953).

(11) See E. J. Corey, G. Slomp, S. Dev, S. Tobinaga and E. R. Glazier, THIS JOURNAL, **80**, 1204 (1958).

(12) All melting points were taken on a micro-hot-stage and are corrected.

(13) The nuclear magnetic resonance spectra were carried out with a 40 megacycle Varian Model 4300-B spectrometer with benzene as the external reference and deuteriochloroform as the solvent. Resonances are reported as shielding value numbers (τ).

violet, but showing bands in the infrared at 6.05 and 11.2 μ in chloroform solution typical of an exomethylene function. Elution of the column with benzene afforded the cyclopropyl ketone V (see below) followed by mixtures of the cyclopropyl ketone V[14] and the 16-methyl-$\pm^{16}$-20-ketone III.[14]

Reaction of the Exomethylene Ketone IV with Potassium Hydroxide.—A solution of 10 mg. of IV in 15 ml. of 5% potassium hydroxide in methanol was refluxed for 2 hours. The solvent was removed *in vacuo*, the residue triturated with water and the crystalline product, after recrystallization from acetone, was identical in all respects with an authentic sample of 3α-hydroxy-16-methyl-16-pregnene-11,20-dione.

Reaction of the Exomethylene Ketone IV with Osmium Tetroxide.—A solution of the exomethylene ketone IV, 90 mg., in 10 ml. of dry dioxane was treated with 90 mg. of osmium tetroxide in 10 ml. of dioxane and allowed to stand at room temperature for 24 hours. The resultant black reaction product was treated with a stream of hydrogen sulfide for 2 hours and then filtered through Celite. Concentration of the filtrate *in vacuo* and crystallization of the residue from ether afforded the furanoid derivative IX, m.p. 204–207°, E_{222} mμ 6,000; $\lambda\lambda_{max}^{chf}$ 5.78, 5.82, 6.0, 6.24 and 9.05 μ. The nuclear magnetic resonance spectrum[13] was in conformity with the assigned structure showing resonances at T = 2.96 (furan olefinic hydrogen) and 7.74 ($CH_3C{=}C-$, with the C bearing O—).

Anal. Calcd. for $C_{24}H_{32}O_4$: C, 74.96; H, 8.39. Found: C, 75.17; H, 8.49.

Maleic Anhydride Adduct X.—A solution of the above furanoid derivative IX, 100 mg. in 10 ml. of benzene, was treated with 80 mg. of maleic anhydride and refluxed for 2 hours. After concentration *in vacuo* the residue was triturated several times with boiling ether and crystalline product, 100 mg., was isolated by filtration. Crystallization from acetone–ether gave the maleic anhydride adduct X as fine needles, m.p. 201–203°; $\lambda\lambda_{max}^{chf}$ 5.40, 5.65, 5.80 and 5.88 μ.

Anal. Calcd. for $C_{28}H_{34}O_7$: C, 69.71; H, 7.10. Found: C, 69.58; H, 7.25.

(14) In the interest of efficient isolation of the cyclopropyl ketone the preferred method is to osmylate the mother liquor first before chromatography (see later experiment above). In this way all unsaturated components are altered in polarity sufficiently to enable easy separation of the desired component.

The maleic anhydride adduct X, 15 mg., was sublimed at 190–195° and 0.05 mm. to give the furan IX.

16,17-Methylenepregnane-3α-ol-11,20-dione Acetate (V).—To a solution of 8.0 g. of mother liquors from the crystallization of III in 100 ml. of dry dioxane was added 6.0 g. of osmium tetroxide in dry dioxane and the reaction mixture was allowed to stand at room temperature for 20 hours. The resultant black solution was treated with a stream of hydrogen sulfide for 2 hours and then filtered. The filtrate was concentrated *in vacuo* and chromatographed on 300 g. of neutral alumina. From the fractions corresponding to 1:1 benzene–petroleum ether through benzene there was obtained, after crystallization from acetone–ether, 950 mg. of the furan compound,[15] m.p. 202–205°. Further elution of the column with benzene through 9:1 benzene–chloroform gave, on concentration and crystallization from acetone–ether, 16,17-methylenepregnane-3α-ol-11,20-dione acetate (V) as mica-like plates, m.p. 171–173°; $\lambda\lambda_{max}^{chf}$ 5.78, 5.83 and 5.93 μ.

Anal. Calcd. for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87. Found: C, 74.46; H, 8.68.

Oxidation of 3α-Acetoxy-16-methyl-16-pregnane-11,20-dione with Potassium Permanganate.—A solution of 1 g. of III in 30 cc. of acetone was treated portionwise with 1.1 g. of potassium permanganate and allowed to stir at room temperature for 2 hours. The reaction mixture was evaporated to dryness, water added andd acidified with sulfuric acid. The excess permanganate and manganese dioxide were discharged with saturated sodium bisulfite. The solution and the acid component were extracted with potassium bicarbonate. The amorphous acid obtained weighed 460 mg. The amorphous acid was identical in the infrared with a sample of acid prepared from the diosphenol VIII by similar oxidation. Treatment of this acid in alkaline solution with a solution of iodine in potassium iodide produced an immediate precipitation of iodofuran.

Oxidation of the Diosphenol VIII to the Acid VII.—A 200-mg. sample of diosphenol VIII in 20 cc. of acetone was oxidized with 261 mg. of potassium permanganate in the manner described above for the oxidation of III. There was obtained 180 mg. of amorphous acid exhibiting the same infrared spectrum as that found for the acid formed from the oxidation of III.

(15) This represents the preferred method of preparation of the furan IX.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

A Useful Model of Optical Activity. I. Open Chain Compounds

BY JAMES H. BREWSTER

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It is suggested that a center of optical activity can usefully be described as a screw pattern of electron polarizability. Patterns which can be described as left-handed screws are dextrorotatory (in the visible), the magnitude of rotation ([M]D) being related to the refractions of the atoms making up the patterns. Empirical rules for predicting the rotatory effects of asymmetric atoms and conformations are presented. A simple method for the conformational analysis of flexible compounds is described; this, together with the empirical rules, allows prediction of the sign and magnitude of rotation of many open-chain compounds.

The establishment of the absolute configuration of tartaric acid,[1] the definitive correlation of configurations in the "carbinyl" series (HCXRR)' with those in the "methine" series (HCRR'R'')[2] and the large body of stereochemical correlations within these two series[3] make feasible an attempt empirically to relate sign of rotation[4] to structure,

(1) J. M. Bijvoet, A. F. Peerdeman and A. J. van Bommel, *Nature*, **168**, 271 (1951).

(2) (a) A. Fredga, *Arkiv. Kemi Mineral. Geol.*, **15B**, No. 23 (1942); (b) K. Freudenberg and J. Geiger, *Ann.*, **575**, 145 (1952); K. Freudenberg and W. Hohmann, *ibid.*, **584**, 54 (1953); (c) D. S. Noyce and D. B. Denney, THIS JOURNAL, **74**, 5912 (1952); **76**, 768 (1954); D. S. Noyce and J. H. Canfield, *ibid.*, **76**, 3630 (1954); (d) J. Trommel, *Proc. Acad. Sci. Amsterdam*, **B57**, 364 (1954); J. Trommel and J. M. Bijvoet, Acta Cryst., **7**, 703 (1954).

(3) For a summary, with many references, see J. A. Mills and W. Klyne in W. Klyne "Progress in Stereochemistry," Vol. I, Butterworths Scientific Publications, London, 1954, pp. 172–222. Most of the configurational assignments used here are discussed in this review.

(4) In the first three papers attention is confined to [M]D values, in part because, for many compounds of interest, no other data are yet available. It is recognized that dispersion measurements which show *experimentally* the location, sign and magnitude of the Cotton effect furnish the most direct method for identifying the rotatory contributions of individual centers of optical activity[7] and should be of value in testing, refining and extending the principles developed here. We are here concerned, however, chiefly with saturated and mono-olefinic compounds, most of which are transparent in the accessible